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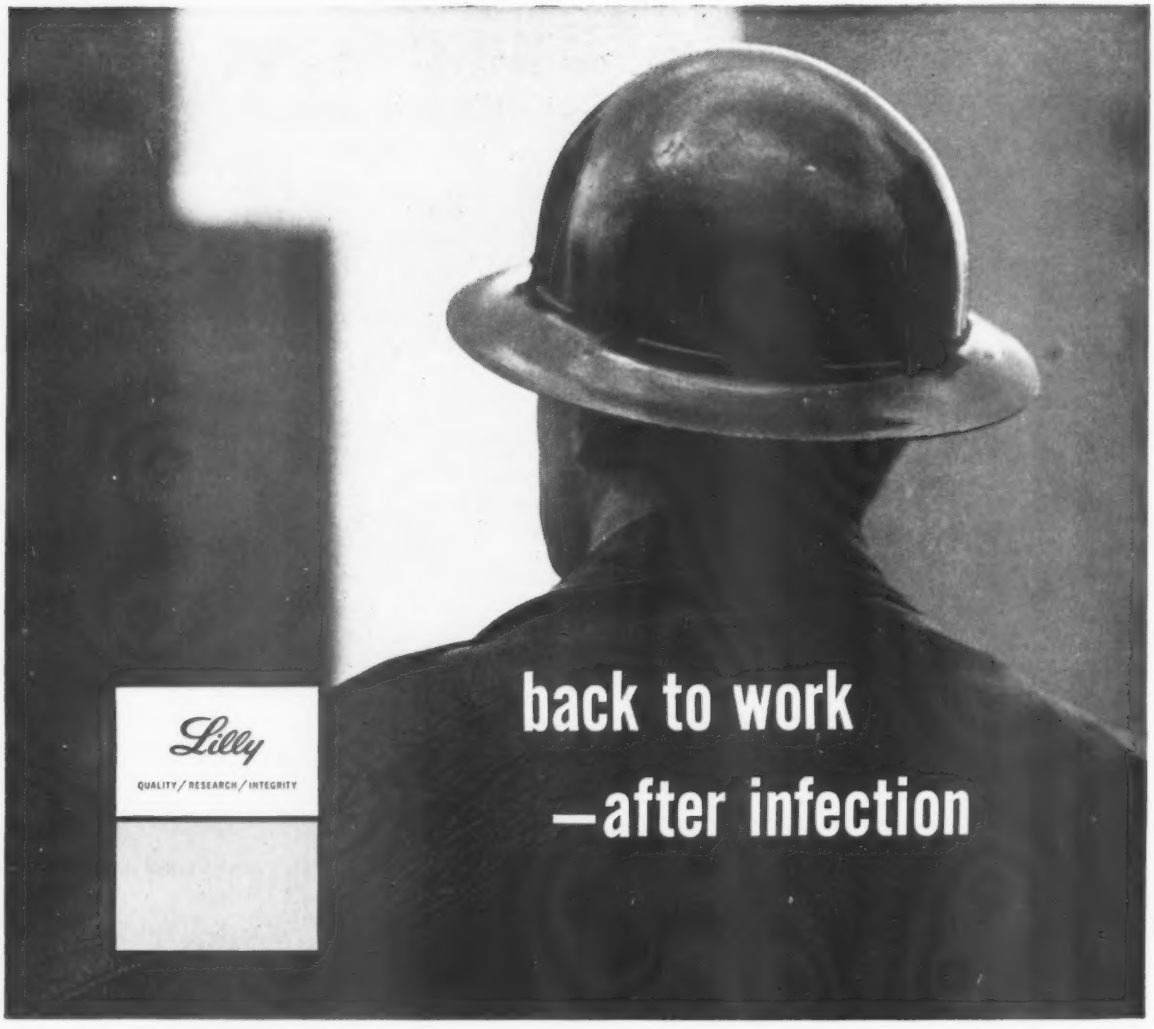

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American Journal of Hospital Pharmacy

American Society of Hospital Pharmacists

VOLUME 17 NUMBER 3 MARCH, 1960

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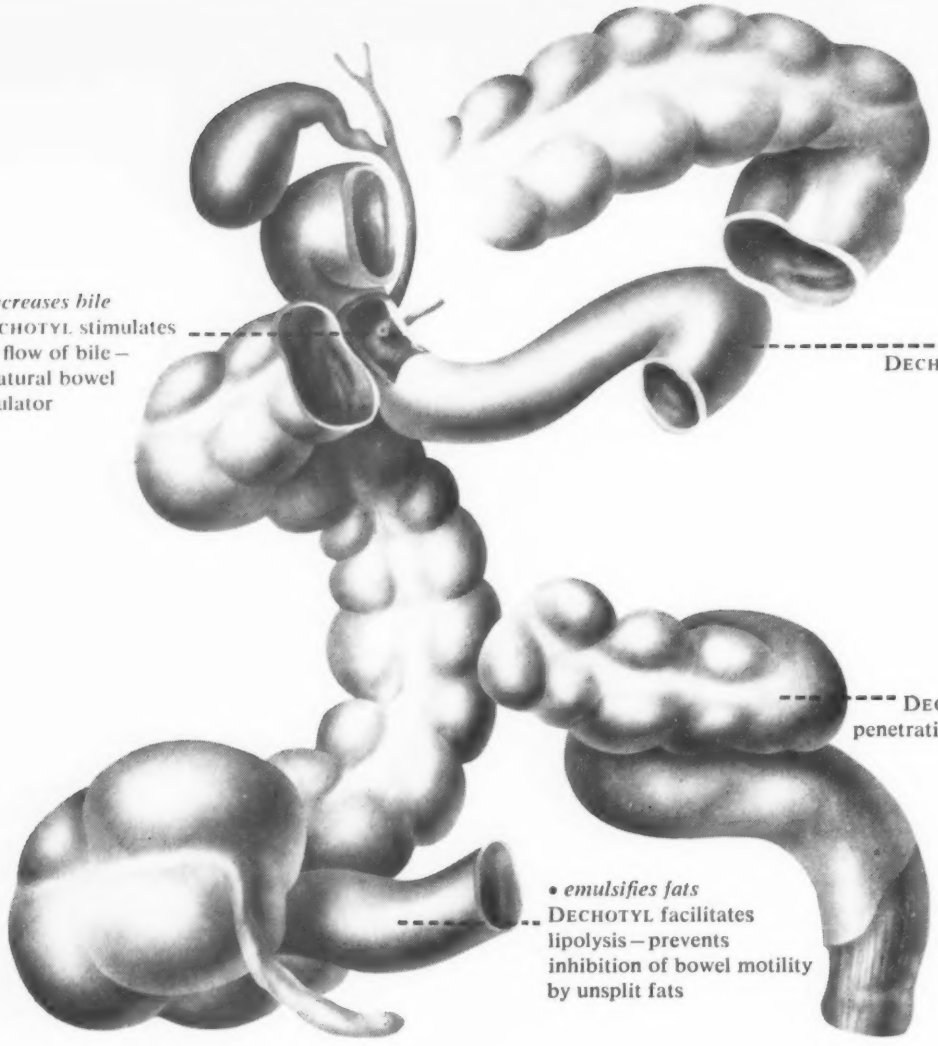

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Garry, M. W.: Am. J. M. Sc. 236:330 (Sept.) 1958.

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1. Garry, M. W., *op. cit.* 2. Editorial, New England J. Med. *261*:152 (July 16) 1959. 3. Nunn, D. B., and Parker, E. F.: Am. Surgeon *24*:361 (May) 1958.

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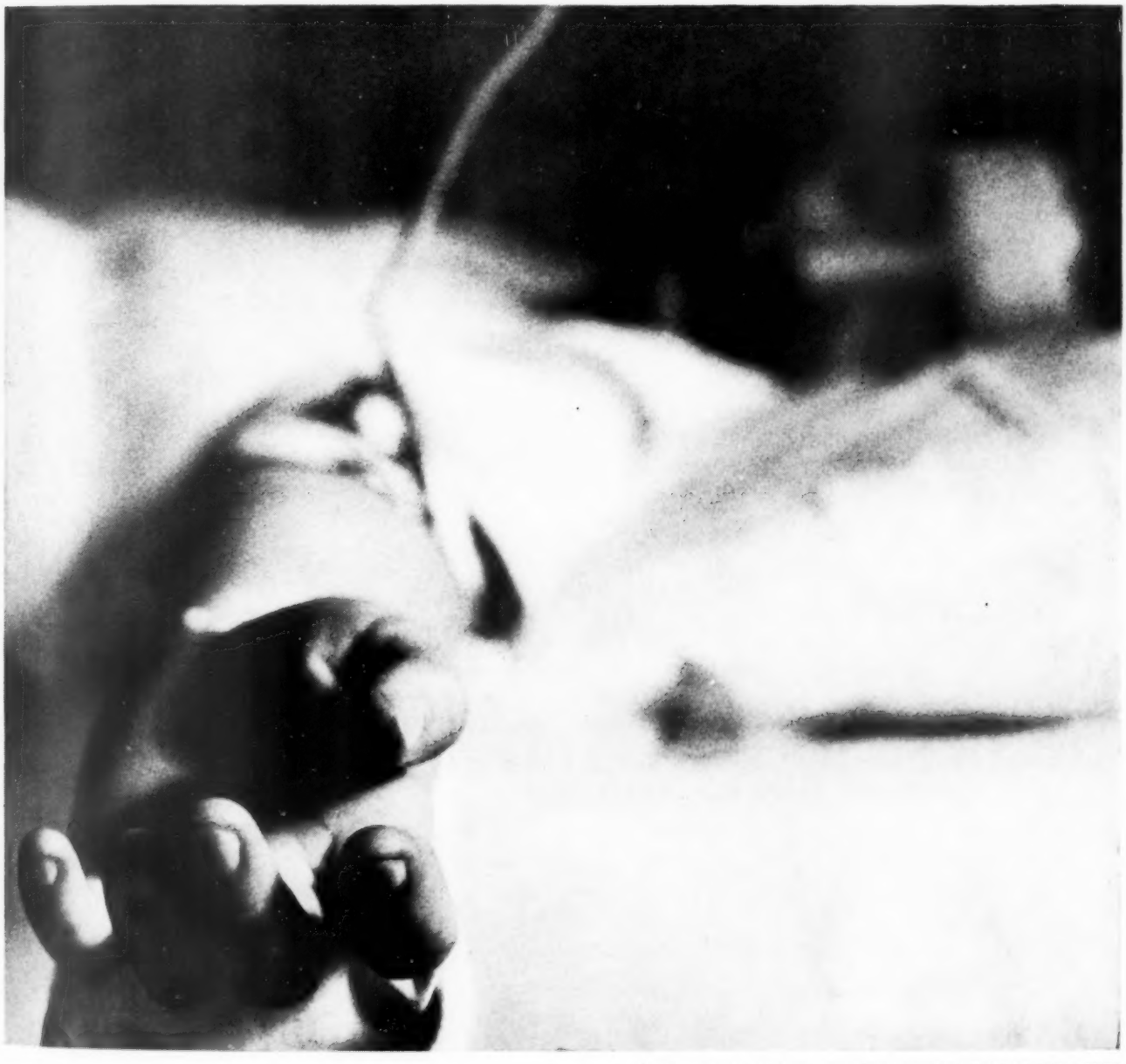

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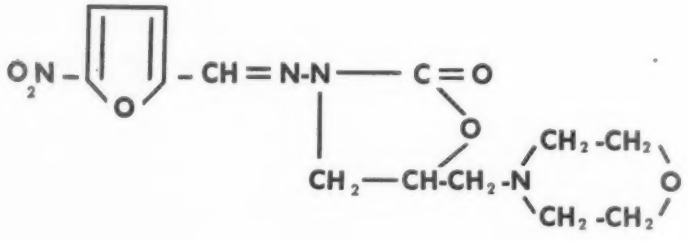

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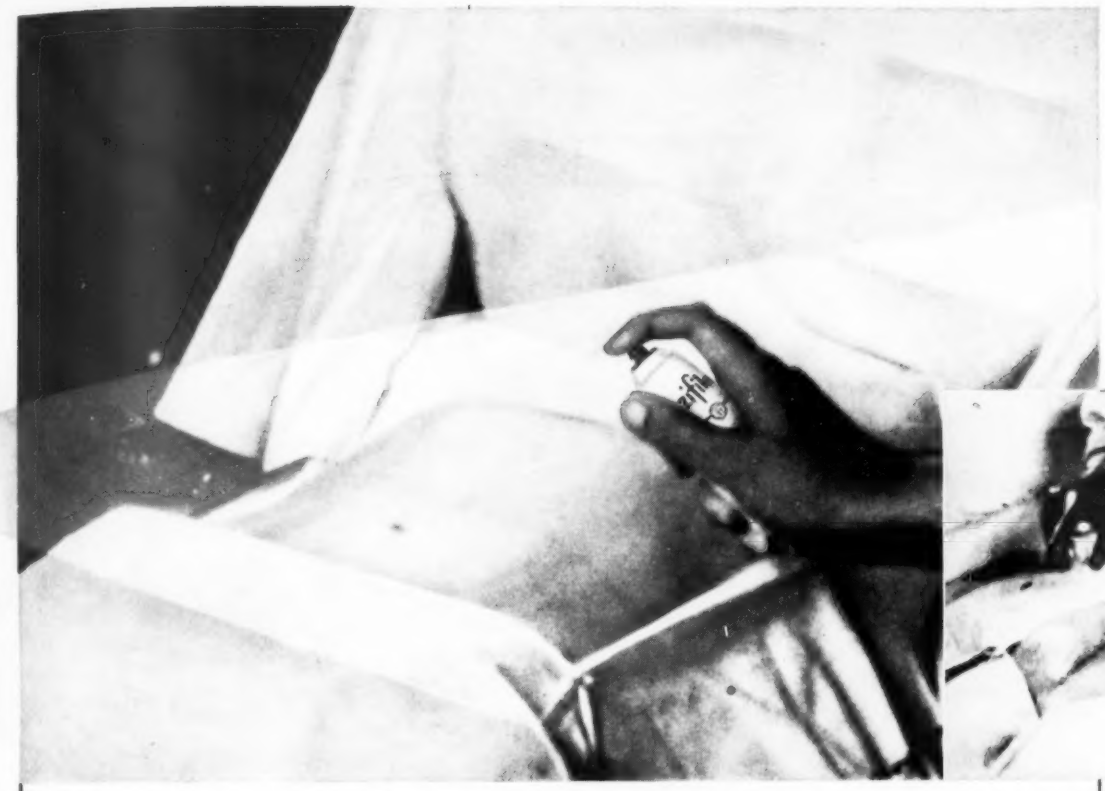
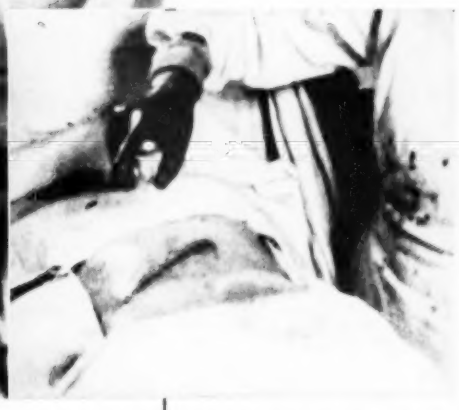
• incision can be made directly through film,[2] minimizing or eliminating need for skin towels • does not impede healing[3] • no sensitization reactions reported • does not interfere with joint movement • more comfortable than adhesive bandages • protects against clothing irritation[4] • protects skin around enterostomy and fistula openings[5]

REZIFILM is *not* indicated as a dressing for second or third degree burns or for bleeding or granulating wounds.

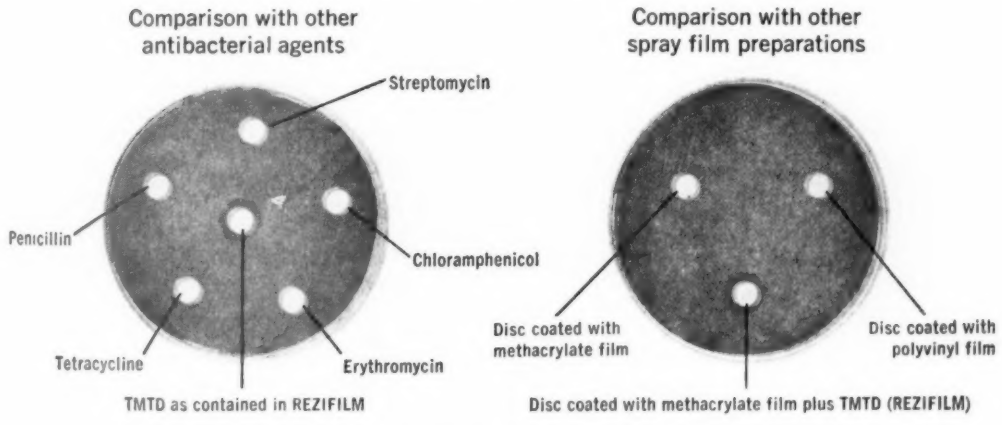


PRE-OPERATIVELY Rezifilm is applied after prepping of the surgical area. It functions as a secondary drape.

POSTOPERATIVELY Rezifilm is applied following final closure of the incision. It provides comfortable protection against infection and irritation.



Compare the antibacterial activity of **REZIFILM**[6]



Streaked cultures of coagulase-positive Staphylococcus aureus, phage type 80/81; incubated 24 hours at 37°C.

An interesting 16 mm. color motion picture film (10 minutes) showing the use of REZIFILM *in surgery is available free of charge. Excellent for hospital and medical society meetings. Write to: Professional Service Department, Squibb, 745 Fifth Avenue, New York 22, N. Y.*

Supplied: 6 oz. (avd.) spray dispenser cans.

References: 1. Eisenberg, G. M.: *Antibiotic Med. & Clin. Ther.*, 6:594 (Oct.) 1959. 2. Thomson, J. E. M.: Report to The Squibb Institute for Medical Research, June, 1957. 3. Maloney, J. V. and Mulder, D. G.: *Am. Surgeon* 23:388 (April) 1957. 4. Bucher, R. M.: Report to The Squibb Institute for Medical Research, July 3, 1957. 5. Hammond, J. A.: Report to The Squibb Institute for Medical Research, May 3, 1957. 6. Eisenberg, G. M.; Weiss, W.; Spivack, A. P.; Bassett, J. G.; Ferguson, L. K., and Flippin, H. F.: Adapted from Scientific Exhibit, A.M.A. Meeting, June 8-12, 1959.

- *provides skin asepsis, both preoperatively and postoperatively*
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"REZIFILM" IS A SQUIBB TRADEMARK

The Administrator's Hidden Asset

How your staff pharmacist can save you Time and Money—even outside the Pharmacy

by Alfred A. Mannino
EXECUTIVE DIRECTOR, HOSPITAL DEPT.
McKESSON & ROBBINS, INC.

Mail response to recent articles in this space has indicated increasing interest in the expanding role of the pharmacist in modern hospital administration. Those who have expressed their own experiences and opinions may be particularly interested in this recent personal experience of my own.

ABOUT a year ago I had lunch with the Administrator of a medium-size Southern hospital. We discussed knotty problems facing hospitals in general. Then we got down to brass tacks and tackled *his* problems.

My friend simply needed more arms and legs! He was besieged with administrative work, and his nursing staff was also overburdened. The old solution, "Just put on your other hat and do your other job," didn't seem to work any longer. More help was needed, there just wasn't any more money—and to increase hospital rates—was a last resort. But he was toying with another possible solution:

"What would you say," he asked, "if I turned some administrative work over to my Pharmacist?"

"I'd say 'Great'!" I enthusiastically replied. "I've seen it work beautifully in hospitals of all sizes—including some that were wondering if they could afford a Pharmacist at all! You see, most Pharmacists graduating today have more than Pharmacy behind their diplomas. They've also studied Drug Marketing, Pharmacy Management, Accounting and Law—as well as Principles of Economics. Older pharmacists have soaked up the same, handling the complex operations of their regular jobs. And I've noticed that most pharmacists, young or old, welcome opportunities to expand responsibilities—and so become more valuable. I think Central Supply would be a good place to start."

My harassed friend needed no further encouragement to start things rolling. So, before leaving town, I briefed our local McKesson Hospital Service Representative and he pitched in with every possible aid.

He also kept me in touch with the situation, but I was eager to see first-hand. So, recently, I returned to the sunny South. Results were so gratifying that I submit them now:

1. Reactions of the hospital staff to the new regime might have presented problems—but not to my Administrator friend. For instance, the veteran nurse who had been doing a conscientious job in Central Supply, first felt she was being demoted. But when the Administrator pointed out his need for ALL her time as Supervisor of Nurses, she brightened up—became fully reimmersed in work *really* close to her heart—and was all for the new setup.

Then, when the Pharmacist (aided by McKesson's local Hospital Service Representative) reorganized Nurses' Stations—ending unbalanced stocks, sudden shortages and frequent back-tracks to Pharmacy, he definitely became Best Friend of the Working Girl—and of everyone else interested in simplifying routines.

2. But the best was yet to come! Taking advantage of McKesson's *full-line* medical stocks and other supplies, the Pharmacist reorganized Central Supply inventory. The better balanced inventory filled all needs fully—without overstocking. Risk of loss through product deterioration or obsolescence was lessened, valuable space was saved—and stock issuing was greatly simplified. Supporting this was the "Rex" McKay® Service—sure to fill all orders intelligently, quickly and with strict adherence to brand specifications. McKesson is, of course, proud of its role in promoting the growth of reliable leading brands.

3. The local McKesson Hospital Service Representative also provided timely surveys. One showed that nurses desire more pharmacological information. Because doctors are often too busy to provide this, a pharmacological training program was set up, with the Pharmacist giving comprehensive talks on each new drug that came into the hospital. Everyone was enthusiastic about this program. The Administrator himself tried to get to every talk.

4. The biggest surprise was the Administrator himself. We had lunch together again, and I found myself seated across from an accomplished speechmaker. It seems he had been relieved of so many burdensome tasks that he initiated a community fund-raising campaign. He had spoken to civic leaders and business men, to church groups and women's clubs. Speechmaking had become so natural that at one point he addressed me as his "distinguished guest." He quickly caught himself and we had a good laugh.

What happened in this hospital is happening in many throughout the country. Administrators are saving time and money by extending the Pharmacist's management activities and purchasing contacts to other aspects of hospital administration. And they are improving hospital services by using the Pharmacist's professional ability in many areas outside pharmacy.

Perhaps this article should have been titled "The Hidden Asset That's Becoming Visible." More and more Administrators are learning to use the valuable asset they have—and an equally impressive number are learning they can afford to acquire such an asset. It's the new trend—and a wonderful illustration of hospital progress.

If you would like more information about how to better utilize a Pharmacist's management and professional assets, one of our McKesson Hospital Service Representatives will gladly help you. Simply address me: A. A. Mannino, McKesson & Robbins, 155 E. 44th St., New York 17, N. Y.

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Brown or hazel iris — 1.0% solution. 15 ml. and 2 ml. dropper bottles.
Blue, gray and green iris—0.5% solution. 15 ml. dropper bottles.
Prolonged therapy — Gel. 3.54 Gm. collapsible tubes.
Samples and literature supplied on request.

References: 1. Miles, P. W.: Missouri Med. *56*:1243, 1959. 2. Costner, A. N.: South. M. J. *48*:1192, 1955. 3. Rasgorshek, R. H., and McIntire, W. C.: Am. J. Ophth. *40*:34, 1955. 4. Gordon, D. M., and Ehrenberg, M. H.: Am. J. Ophth. *38*:831, 1954.

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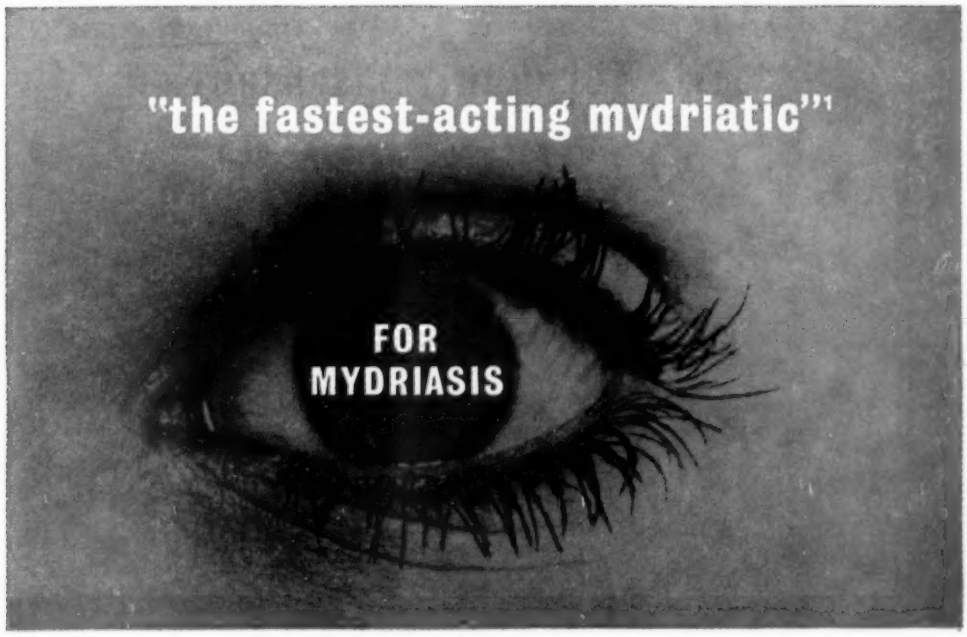

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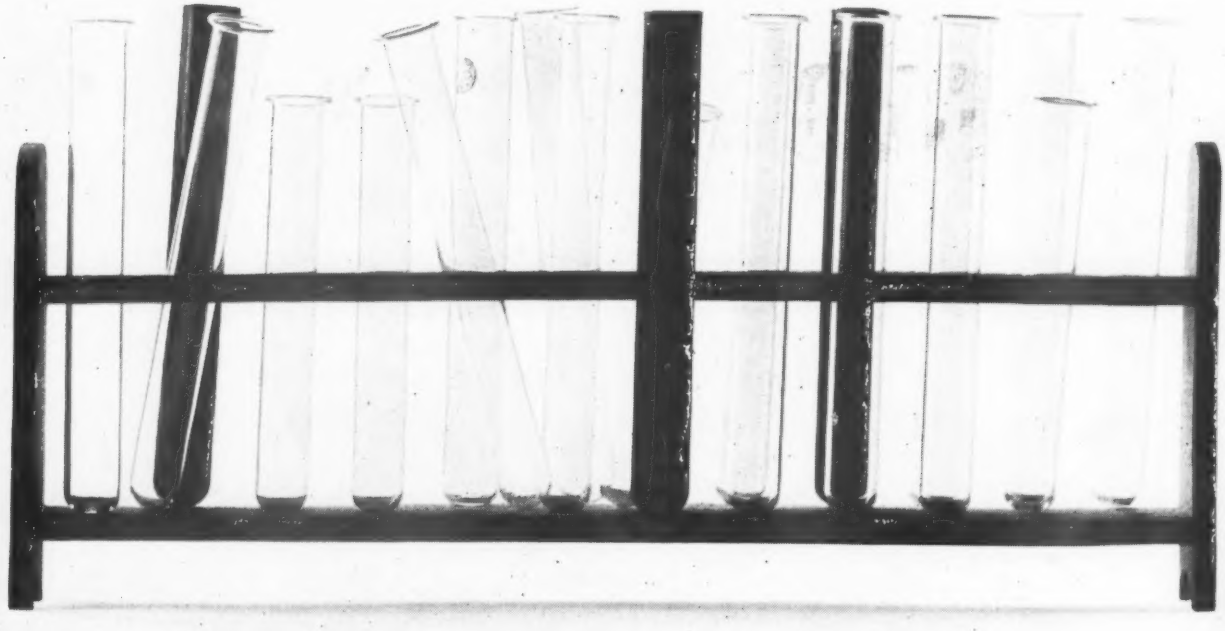

1. Romansky, M. J.. Ristocetin, Antibiotics Monographs, No. 12, New York, Medical Encyclopedia Inc., 1959.

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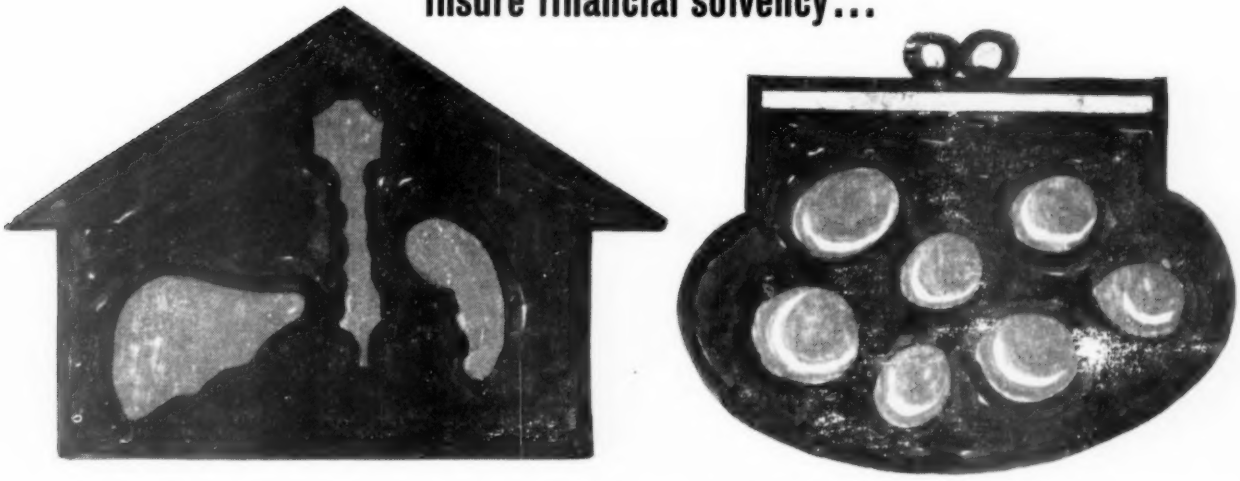

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(1) Holly, R. G.: Postgrad. Med. **26**:418, 1959. (2) Evans, L. A. J., in Wallerstein, R. O., and Mettier, S. R.; Iron in Clinical Medicine, Berkeley, Univ. California Press, 1958, p. 170. (3) Schwartz, L.; Greenwald, J. C., and Tendler, D.: Am. J. Obst. & Gynec. **75**:829, 1958.

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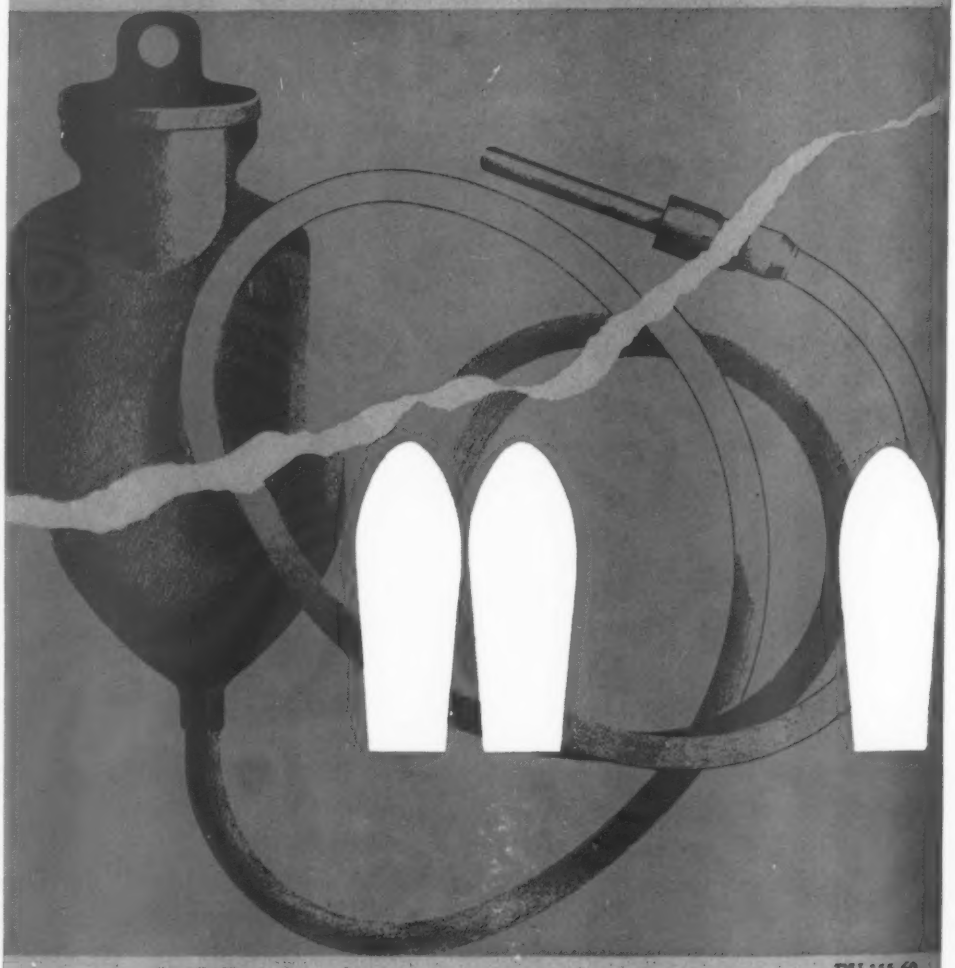

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Northern California Society

The Tao Tao Restaurant in San Francisco was the scene of the installation dinner for officers of the Northern California Society of Hospital Pharmacists on January 12. Officers installed at this meeting were: *President* William Dudley; *Vice-President* Charles Jackson; *Secretary* George Gruber; and *Treasurer* Ellen Berlin.

In his acceptance address, President Dudley spoke of the relationships of the hospital pharmacist with others in his profession, the ethics of filling outpatient prescriptions, and the formulary system.

A special guest at the dinner was Dean Ivan Rowland, of the College of Pharmacy at the College of Pacific, Stockton, California.

Southern California Society

Wendell T. Hill, Jr., Chief Pharmacist at the Orange County General Hospital, was installed as President of the Southern California Society of Hospital Pharmacists at the Annual Installation Banquet held on January 13 in Los Angeles.

Other officers installed at this time were: *Vice-President* Chester Bazel, Veterans Administration Center; *Secretary* Jean Jarvis, Long Beach Community Hospital; and *Treasurer* Kiku Munemori, St. Vincent's Hospital, Los Angeles.

The principal speaker for the evening was Mr. Charles Simmons II of the Simmons Institute in Los Angles.

At a recent meeting of the Executive Committee of the Southern California Society, plans were made to honor Sister Mary Junilla by presenting a plaque to Queen of Angels Hospital where Sister Junilla was Chief Pharmacist for many years.

1960 Officers of the Southern California Society of Hospital Pharmacists. Shown left to right are: President Wendell T. Hill; Secretary Jean Jarvis; Vice-President Chester Brazel; and Treasurer Kikuyo Munemori

Colorado Society

The regular meeting of the Colorado Society of Hospital Pharmacists was held on December 23 at the University Memorial Center in Boulder, Colorado.

The meeting opened with a discussion on the forthcoming Seminar which will be held in April. A questionnaire has been sent throughout the state asking for suggestions regarding the type of program wanted.

Other topics discussed at this meeting were those of recruiting people into the profession of pharmacy and the best programs to be used in recruitment, and the problems of drug displays in hospitals by detail men.

Officers of the Colorado Society elected to serve during 1960 are *President* Joseph LaNier, National Jewish Hospital, Denver; *Vice-President* Irvin Friesen, Porter Sanitarium and Hospital, Denver; and *Secretary-Treasurer* Margie Gaasch, University of Colorado Medical Center, Denver.

Illinois Society

The Illinois Society of Hospital Pharmacists met on January 12 at the St. Clare Hotel in Chicago.

At the request of the Illinois Hospital Association, a member of the Society was appointed as a representative to that group. Mr. Charles Lev was selected as the representative.

The program for the evening was a panel discussion moderated by Mr. Edgar Duncan. The panelists included Mr. Meyer Mitchnik, Mr. Samuel Bilicke, Mr. Edward Hartshorn, and Mr. Peter Solyom. The subject for discussion was "Problems of Hospital Pharmacists," and included such considerations as professional associations, relationship between hospital pharmacists and medical service representatives, and after-hours service in the pharmacy.

The Executive Committee of the Illinois Society of Hospital Pharmacists met on January 26 for a discussion of the program for the Society for the balance of the year.

In addition to programming, other items discussed included the survey on the use of radioisotopes, the forthcoming Seminar at the University of Illinois, and the Annual Student Visitation Program.

Indiana Chapter

The regular quarterly meeting of the Indiana Chapter of the American Society of Hospital Pharmacists was held in conjunction with the Indianapolis Branch of the American Pharmaceutical Association on January 16 at the Indiana University Student Union Building in Indianapolis.

The seminar-type program presented the following topics and speakers:

Report of the House of Delegates, Mr. J. Warren Lansdowne, Chairman, American Pharmaceutical Association House of Delegates.

"Isotopes—Their Role in Pharmacy," Dr. John Christian, Purdue University School of Pharmacy.

"The Heart, and Drugs Used in the Treatment of Heart Disease," Dr. A. D. Dennison, Jr., Indianapolis.

"Let's Act Now," Mr. Paul A. Pumpian, Secretary, Wisconsin State Board of Pharmacy.

"Poliomyelitis Vaccine in 1960," Dr. Robert C. Warner, Associate Medical Director, Pfizer Laboratories.

In the business meeting which followed the program, the Indiana Chapter voted to sponsor the Pharmacy Section of the Tri-State Hospital meeting in 1961.

Continuing the Joint Meeting with the Indianapolis Branch in the evening, a reception and dinner was held at the Indiana University Student Union Building. Dean Lloyd Parks of the Ohio State University School of Pharmacy, spoke on "Recruitment Is Your Business."

Massachusetts Society

On February 17 the members of the Massachusetts Society of Hospital Pharmacists met at the offices of McKesson and Robbins, Inc., Boston, for their regular meeting. Mr. Alfred A. Mannino, Sales Manager for the Hospital Department, was speaker for the program.

During the business portion of the meeting, the members voted on proposed changes in the Constitution and By Laws.

Maryland Association

The Maryland Association of Hospital Pharmacists installed new officers at a dinner meeting held at the Sheraton Belvedere Hotel in Baltimore on January 21. Officers who will serve for 1960 are: *President* Robert A. Statler; *Vice-President* Robert E. Lawson; and *Secretary-Treasurer* Mary W. Connelly.

Mr. Paul Freeman, Manager of Professional Relations for E. R. Squibb and Sons, was the speaker for the evening. His topic was entitled "New Weapons Against Disease."

Michigan Society

On January 5 the Michigan Society of Hospital Pharmacists met for its regular meeting at the William Beaumont Hospital in Royal Oak.

The program for the evening was a discussion and film on radioactive isotopes. The film was prepared by Abbott Laboratories in conjunction with William Beaumont Hospital.

St. Louis Association

The Hospital Pharmacists' Association of Greater St. Louis met for its regular meeting on January 12 at St. Mary's Hospital.

Dr. C. Lee Huyck reported for the Educational Committee that the Annual Refresher Course will be held at the St. Louis College of Pharmacy on April 21. A course dealing with the more scientific principles will be held later in the year.

The St. Louis Society is in the process of preparing a list of the hospitals in the local area along with information relating to the scope of the pharmacy service and the names of the pharmacy staff.

New Jersey Society

The members of the New Jersey Society of Hospital Pharmacists met at the Elizabeth General Hospital on January 21. The program for the evening was presented by the Upjohn Company, and consisted of a film on the production and use of hydrocortisone.

A business meeting followed presentation of the film. It was announced that the Pharmacy Committee of the New Jersey Hospital Association had requested the formation of a Task Committee to survey the cost of drugs in hospitals. Such a study has been made necessary by the results of a recent survey by Blue Cross which disclosed that the cost of drugs is less in hospitals which do not employ pharmacists.

The plan for the Committee is to have committees of the New Jersey Society of Hospital Accountants and the New Jersey Society of Hospital Pharmacists meet and formulate standard accounting procedures in hospitals, and survey the various drug costs in hospitals. The New Jersey Hospital Association will sponsor a seminar for pharmacists and accountants.

Greater New York Chapter

Sister Mary Bernadine of New York Foundling Hospital was elected President of the Greater New York Chapter of the American Society of Hospital Pharmacists at the meeting on January 19 at St. Mary's Hospital in Brooklyn.

Other officers elected were: *Vice-President* Sister Mary Etheldreda, St. Mary's Hospital: *Recording Secretary* Sister Mary Rita, Frances Schervier Home and Hospital: *Correspond Secretary* Sister Mary Angeline, St. Mary's Hospital; and *Treasurer* Sister Mary Donatus, St. Clare's Hospital.

The guest speaker for the afternoon was Mr. B. J. Saccomanno of Lederle Laboratories. His subject, "Chelates and Chelation," covered the uses of chelates in medicine and pharmacy as well as industry. The future possibilities of chelates were discussed also.

Northeastern New York Society

The Northeastern New York Society of Hospital Pharmacists met January 22 at the Veterans Administration Hospital in Albany.

The business for the evening was the planning of the program for a Seminar to be held early in April. Mr. Louis Jeffrey was appointed Chairman for the event.

Southeastern New York State Chapter

The Southeastern New York State Chapter of the American Society of Hospital Pharmacists met at The New York Hospital on December 16.

Business conducted at the meeting included reports from the Membership Committee, Program Committee, and Special Projects Committee. The Program Committee outlined the programs to be given in the coming year, and the Special Projects Committee offered for consideration several projects for the chapter. Among the plans discussed were Development of a Code of Ethics for Hospital Pharmacy in Dealing with Pharmaceutical Representatives, Hospital Pharmacist Job Descriptions, and Interviewing Job Applicants.

The program for the evening was presented by Dr. Lester Luntz, Training Director at New York Hospital. Dr. Luntz spoke on "Rating and Job Coaching." This presentation was followed by an open discussion on the topic.

Akron Area Society

The Akron Area Society of Hospital Pharmacists met at St. Joseph Riverside Hospital in Warren, Ohio on January 12. Final plans for the program for the Student Project were presented. The Student Project this year will be held on April 19 and 20.

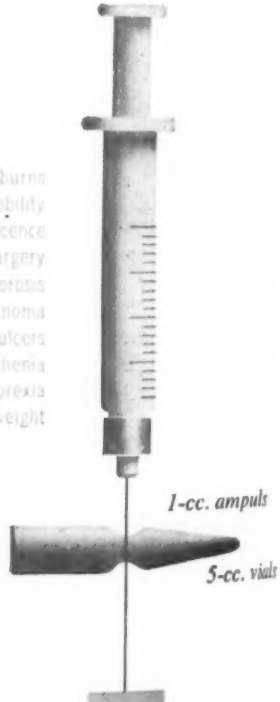
Also included in the business session was a discussion of plans for the annual student project which is scheduled for April 19 and 20. With a Committee headed by Mary Morgan, students from Schools of Pharmacy in the area are invited to visit hospitals in Akron and to attend a regular meeting of the Akron Area Society.

CONTINUED ON PAGE 30

1 cc.

once each week

burns
debility
convalescence
surgery
senile osteoporosis
mammary carcinoma
decubitus ulcers
asthenia
anorexia
underweight



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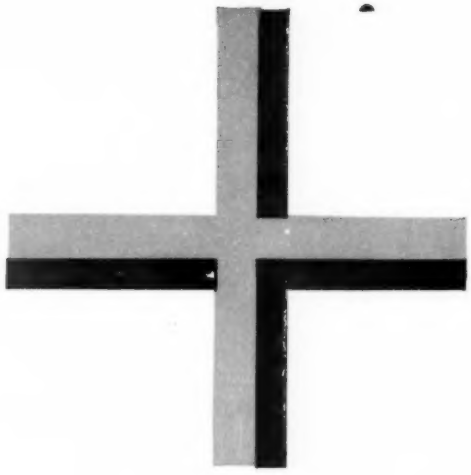

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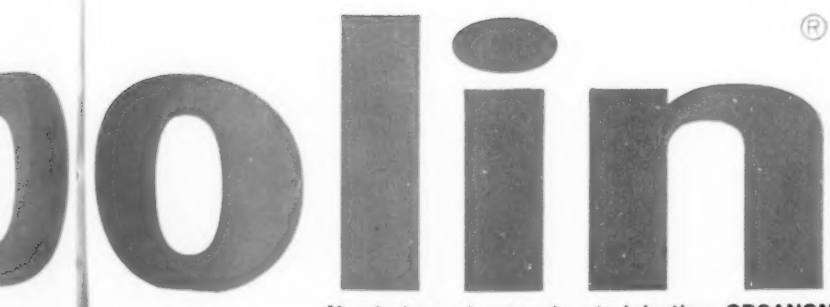

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Cleveland Society

The Cleveland Society of Hospital Pharmacists met on January 27 at the offices of the Cleveland Hospital Council.

Final plans were formulated for the trip to the laboratories of E. R. Squibb and Sons in New York. The dates for the tour will be March 16 and 17.

Mr. Frank A. Hayba of the Cleveland Hospital Council was the speaker for the evening. He discussed the background and present functions of the Council.

Oklahoma Society

The first meeting of 1960 for the Oklahoma Society of Hospital Pharmacists was held at St. Anthony Hospital in Oklahoma City on January 21.

Mr. William Kelly of Lederle Laboratories was the speaker for the evening. The title of his presentation was "Values of Health."

In the business meeting which followed, committee members were appointed to the following committees: Program, Constitution and By Laws, and Resolutions.

Houston Area Society

The Houston Area Society of Hospital Pharmacists met on January 17 to install new officers for 1960. The new officers are: *President* H. A. McIntosh; *Vice-President* Jack Farmer; and *Secretary-Treasurer* Minnie Jones. The officers were installed by Mr. Robert Lantos and Miss Adela Schneider.

Mr. Paul Hudson, out-going president, introduced the speaker, Dr. John Stover of the Internal Medicine Department of the Veterans Administration Hospital in Houston. Dr. Stover discussed drugs currently used in the treatment of tuberculosis. An open discussion period followed the presentation.

The November meeting of the Houston Area Society was held at St. Luke's and Texas Children's Hospital. The program for this meeting was a presentation by Mr. Paul Wilburn and Miss Adela Schneider on the "History of the Texas Medical Center."

In October the Society met at the Methodist Hospital in Houston. The principal topic of business at this meeting was a proposal that the Texas Society of Hospital Pharmacists form a section of the Texas Pharmaceutical Association. This proposal was reported and discussed by Mr. Robert Lantos.

Utah Society

The regular meeting of the Utah Society of Hospital Pharmacists was held at the Country Club in Salt Lake City on January 18. The meeting preceded the annual Robins dinner.

Topics discussed during the meeting included changes that are to be made in the Constitution and By-Laws. A Committee has been appointed to make a study of the proposed changes and report at the next meeting.

In December the Utah Society held its annual Christmas Party at the Hillside House in Farmington, Utah.

The November meeting was an educational meeting held at the Utah Valley Hospital. The program for the evening was a presentation on mental disease. A film, "As Others See Us," was shown as a part of the program.

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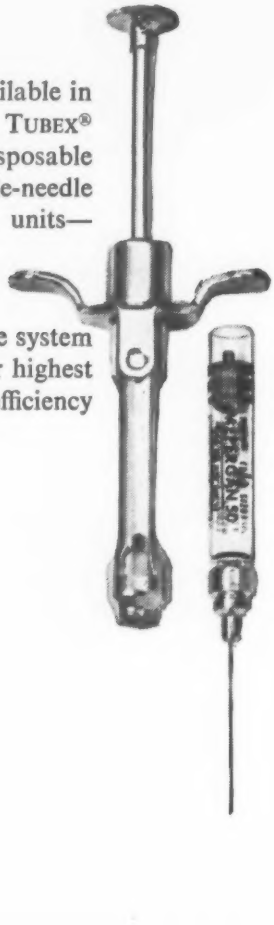

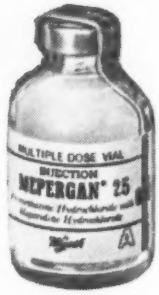

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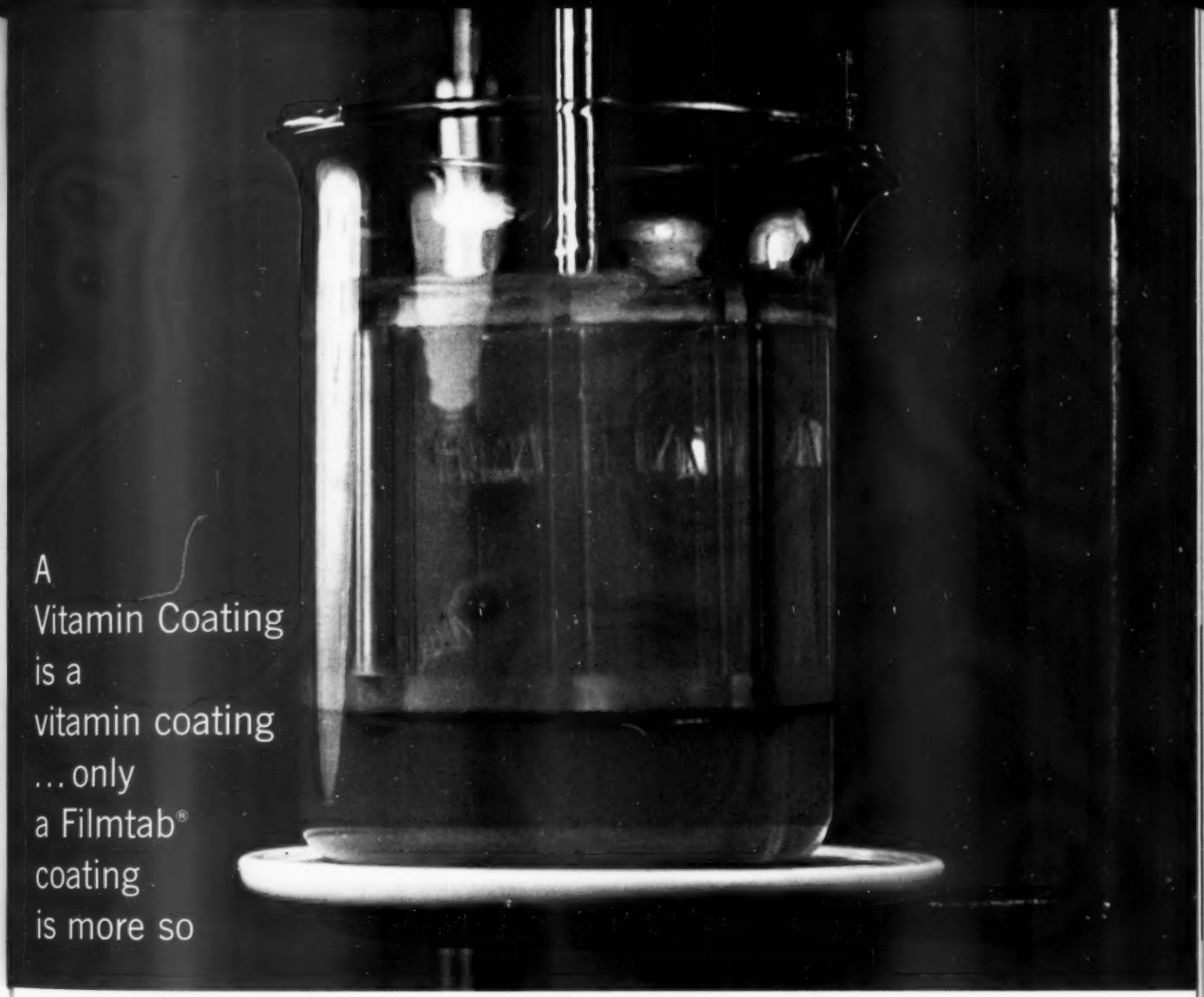

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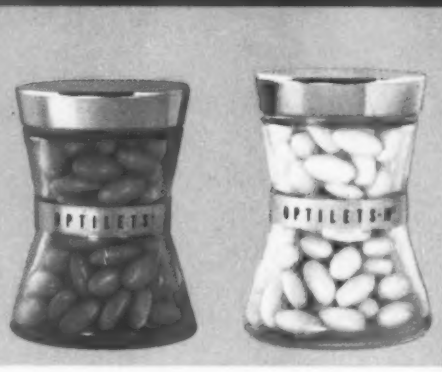

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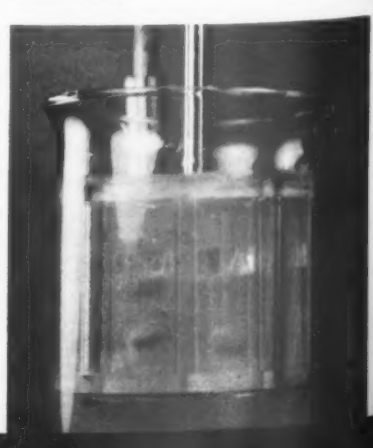

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1. Garnes, A. T., et al.: Am. J. Surg. 97:29, 1959.

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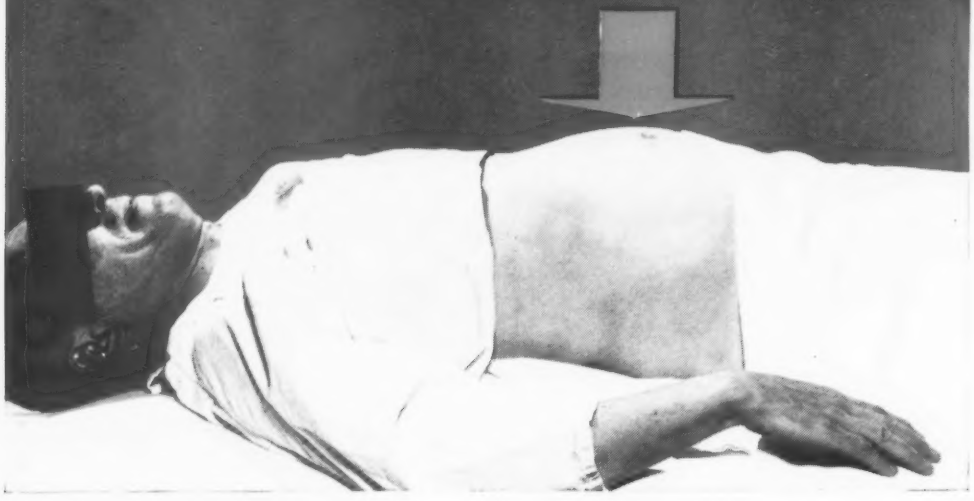

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1. Kareha, L. G., de Quevedo, N. G., Tighe, P., Kehrli, H. J., "Evaluation of Ilopan in Postoperative Abdominal Distention," Western J. Surg. Obs. & Gyn., 66:220, 1958.
2. Stone, M. L., Schlussel, S., Silberman, E., Mersheimer, W. L., "The Prophylaxis and Treatment of Postpartum and Postoperative Ileus with Pantothenyl Alcohol," Amer. J. Surgery, 97:191, 1959.

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REFERENCES: 1. Compilation of Clinical Reports, Department of Clinical Investigation, Lederle Laboratories, January, 1960. **2.** Duke, C. J.; Katz, S., and Donohoe, R. F.: Paper read at Seventh Antibiotics Symposium, Washington, D. C., November 5, 1959. **3.** Floyd, R. D., and Anlyan, W. G.: Clinical report, cited with permission. **4.** Prigot, A.; Maynard, A. de L., and Zach, B.: The Treatment of Soft Tissue Infections with Demethylchlortetracycline. To be published.

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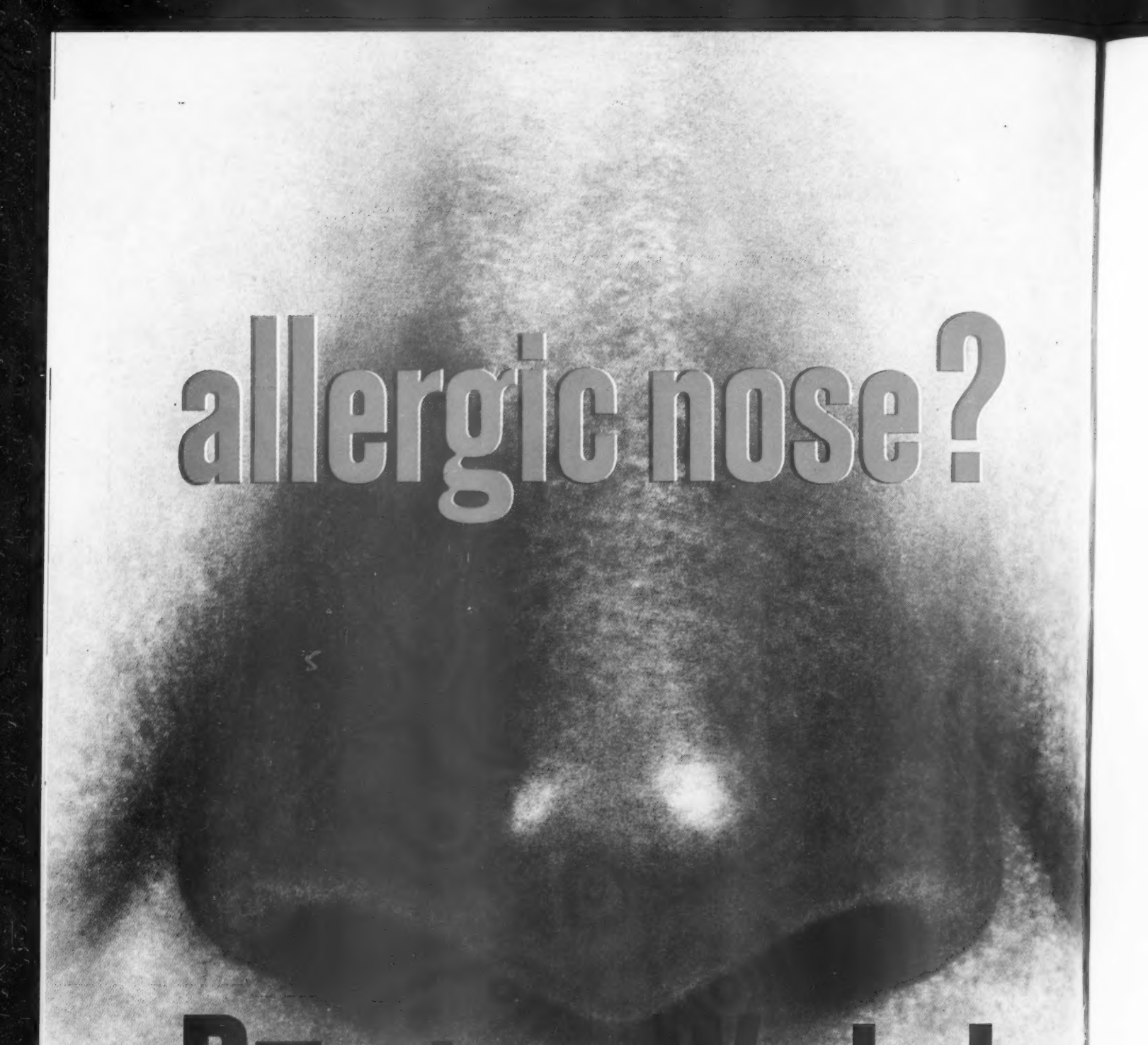

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—New England J. Med. *261*:478, 1959 (Schiller, I. W. and Lowell, F. C.)

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Take a Close Look at Hospital Injectables

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There is little doubt that disposable equipment has assumed great importance in the modern hospital. Certainly, no hospital administrator would dispute the fact that disposable items such as knife blades, blood lancets, urine collection bags, catheters, and enemas all help increase efficiency and, often, cut costs.

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The benefits that the TUBEX system brings to hospital personnel, and the contributions that it makes to hospital efficiency and the welfare of patients, are impressive. Consider, if you will, the following examples.

1. Accurately measured dose assured
2. Danger of giving wrong drug reduced

Each sterile cartridge-needle unit contains an accurate, clearly labeled dose. Therefore, the nurse no longer must measure out doses as before—perhaps from an often-used, possibly contaminated multiple-dose vial. She runs little risk of administering an inaccurate dose or, worse yet, the wrong drug entirely. Obviously, the less chance for error the fewer the number of malpractice suits.

3. Efficiency of Central Supply increased
4. Breakage losses reduced

TUBEX cartridge-needle units are pre-sterilized; the needles pre-sharpened. This means that Central Supply can turn its attention to duties other than the time-consuming sterilization of syringes and the sharpening and sterilization of needles. It also means that breakage, which invariably accompanies these operations, and which raises the hospital's costs, is drastically reduced.

5. A source of hepatitis eliminated
6. Contact sensitization minimized

TUBEX cartridge-needle units serve for a single injection only. There can be no contaminated needles to transmit serum hepatitis or other diseases. Also, because there is virtually no chance for spillage, the nurse rarely comes into contact with drugs that might produce dermatitides or be absorbed to cause even more serious effects.

7. Inventory control simplified
8. Narcotic security tightened

The TUBEX system requires only two parts, half as many as the "conventional" system.

TUBEX System: cartridge-needle unit, syringe
Conventional System: plunger, barrel, needle, medication

There are fewer records to keep. Inventory control, therefore, is more accurate and efficient. As inventory control becomes more accurate, narcotic security automatically tightens.

9. Patients react more pleasantly to injections
10. Most commonly used drugs available

The most obvious direct benefit that the TUBEX system provides for the patient is a relatively painless injection, the result of a fresh, pre-sharpened, single-use needle. Since most common drugs—and many uncommon ones as well—are available in TUBEX form, the majority of hospital patients can benefit from the TUBEX system.

11. Accounting made more efficient
12. Billing made more accurate

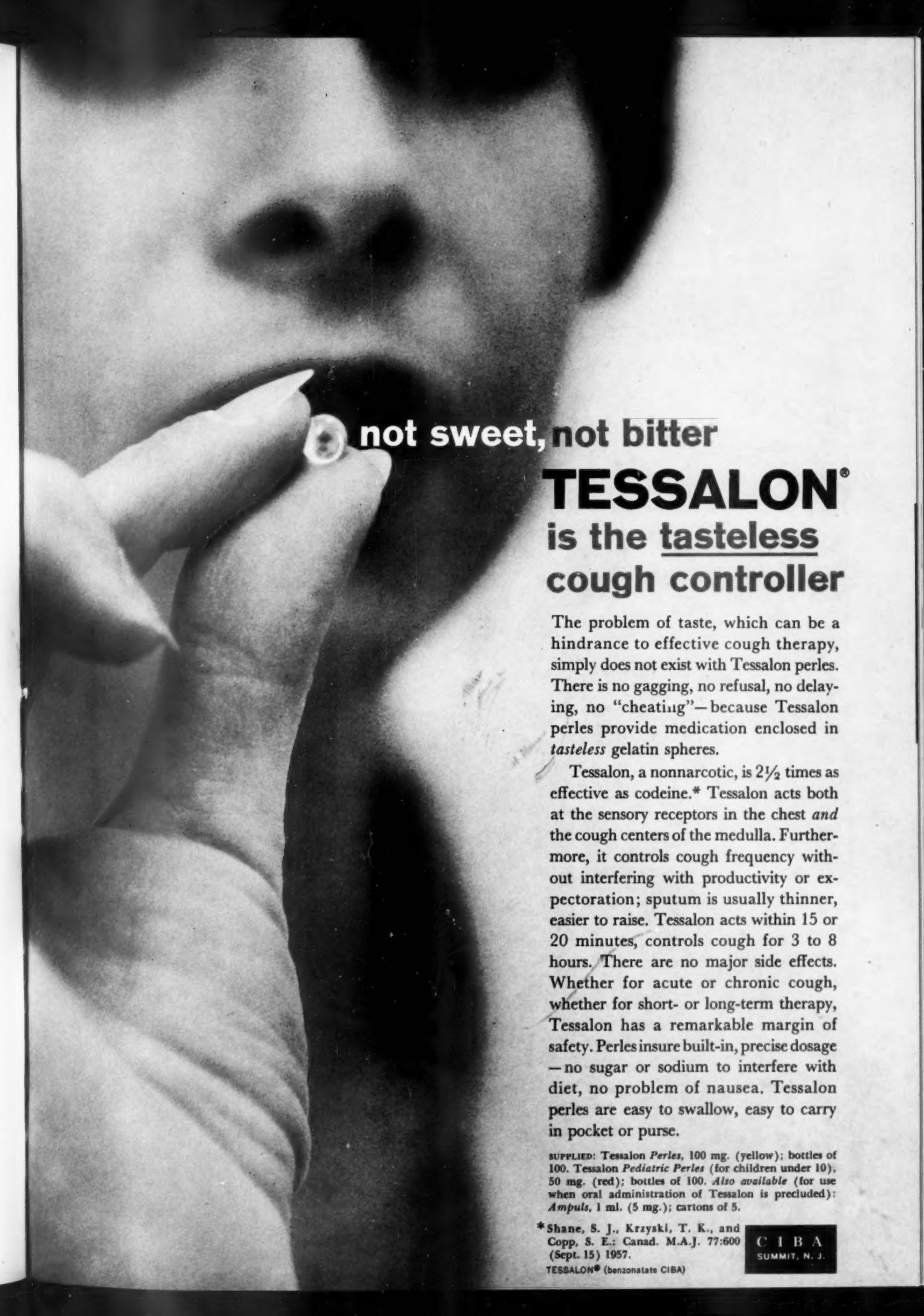
Since each cartridge-needle unit contains a single, pre-measured dose, the amount of medication, including narcotics, that is given a patient is readily ascertainable. Hence, accounting is facilitated and the proper charges to the patient can be made accurately and easily.

In summary

As you can see, adoption of the TUBEX system can have far-reaching effects. Efficiency and morale of the staff are improved. Labor costs—currently about 70 cents of every dollar spent by the hospital—are markedly reduced. Accounting, billing, and inventory control are made more accurate. The risk of malpractice suits is mitigated. The well-being of patients is enhanced.

The TUBEX system can presently supply more than 75 per cent of injectables commonly administered in hospitals. And medications not yet available in TUBEX form can be administered by means of empty, sterile cartridge-needle units. Thus, the TUBEX system is capable of meeting every need for injectables.

The TUBEX system is already in wide use. To learn more about the many benefits that the TUBEX system can bring to *your* hospital, please see your Wyeth Territory Manager or write to Wyeth Laboratories, P.O. Box 8299, Philadelphia 1, Pa.



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*Shane, S. J., Krzyski, T. K., and Copp, S. E.: Canad. M.A.J. 77:600 (Sept. 15) 1957.

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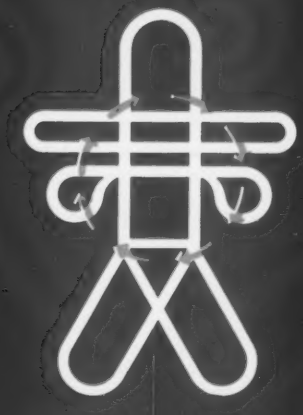

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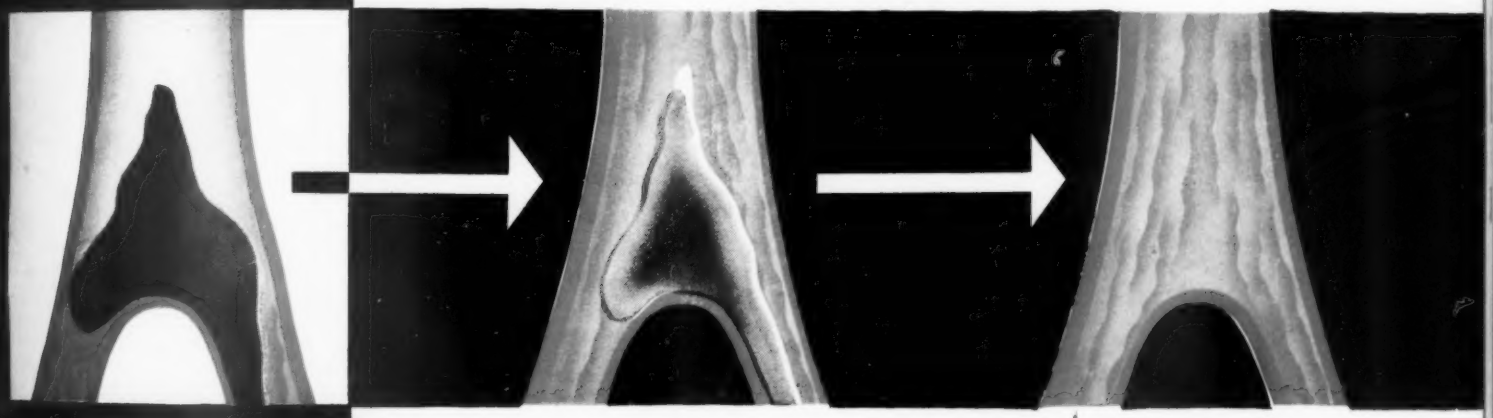
R CLOTS

in thrombophlebitis and pulmonary embolism



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1. McInnes, G. F.; Engler, H. S., and Saliba, N. R.: To be published. 2. Samuels, M. L.; Stehlin, J. S.; Dale, S. C., and Howe, C. D.: South. M. J. 52:207, 1959. 3. Coblentz, A., and Bierman, H. R.: New England J. Med. 255:694, 1956.

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Dear Sirs:

From India

DEAR SIRS: Thank you very much for sending copies of the AMERICAN JOURNAL OF HOSPITAL PHARMACY... They have been a tremendous help in connection with our pharmacy problems, including policies, inventory control, formulary, and ophthalmic solutions. Also helpful is the information on new drugs...

SISTER M. JANE FRANCES, *Pharmacist*

Kurji Holy Family Hospital
P.O. Sodaquat Ashram
Patna, Bihar, India

Praise for Editorial

DEAR SIRS: May I offer a word of praise for your editorial "The Law of Reasonableness Applies" which appeared in the January issue of the AMERICAN JOURNAL OF HOSPITAL PHARMACY. I think it gives the hospital pharmacist a logical explanation as to why the formulary system for hospitals is sound in principle.

CHARLES N. MAY, *Assistant Professor of Hospital Pharmacy*

The University of Georgia
School of Pharmacy
Athens, Georgia

DEAR SIRS: Your editorial entitled "The Law of Reasonableness Applies" certainly sounds reasonable to me.

WILLIAM M. HELLER, Ph.D., *Chief Pharmacy Service*

University of Arkansas
Medical Center
Little Rock, Arkansas

Interest in Liability Insurance Program

DEAR SIRS: The Akron Area Society of Hospital Pharmacists discussed the liability insurance program sponsored by the ASHP at a recent meeting. The group, as a whole, thought this a very fine thing for the national SOCIETY to do. Some of the members did express regret that they had renewed their own liability policies and would not be able to take advantage of this offer for another year. However, as a group, we would like the people at the national level, who have worked hard to make the program possible, to know we appreciate their efforts.

CORRINE RHO, *Secretary*

Akron Area Society of Hospital Pharmacists
Akron, Ohio

DEAR SIRS: ... the officers and members of the Northern California Society of Hospital Pharmacists are pleased with the recent action of the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS in making available a low cost comprehensive malpractice insurance for its members.

GEORGE J. GRUBER, *Secretary*

Northern California Society of Hospital Pharmacists
San Francisco, California

EDITOR'S NOTE: A plan for providing a professional liability insurance program for members of the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS was adopted at the 1959 Annual Meeting. Official announcement of the program was made in the November (1959) issue of the AMERICAN JOURNAL OF HOSPITAL PHARMACY (page 605) and all members have received a communication giving details. The program is offered through the firm of Maginnis and Associates, Inc. of Chicago. Members of the ASHP wishing to participate in the program may direct inquiries to: Maginnis and Associates, Inc., Insurance Consultants, 327 South LaSalle Street, Chicago 4, Illinois.

From Australia

DEAR SIRS: ... replying to your question about our Society, here are a few facts which may be of interest to you. Although the Society is "of Australia," only two of the States, Victoria and Western Australia, have active divisions. Here in Victoria, we have about 100 members...

The Society was inaugurated in Victoria in 1941, and has continued to flourish ever since. Its success is perhaps best illustrated by the superior status and conditions of employment enjoyed by hospital pharmacists in this State. However, we are at the moment actively engaged in an attempt to federate the Society.

Thank you for your offer to exchange THE JOURNAL of your SOCIETY for a similar publication of this Society. Unfortunately, we have no publication, but several members of our Society, myself included, have a subscription to the AMERICAN JOURNAL OF HOSPITAL PHARMACY and find it to be of great interest and value.

I hope that one day in the not too distant future, representatives of our Society may be able to visit the United States and learn, at first hand, of the great organization for hospital pharmacists in the U.S.A.

Once again our thanks for your assistance.

E. BARRY DEAN, *President*

Society of Hospital Pharmacists of Australia (Victoria Division)
Box Hill and District Hospital
Box Hill, E. 11, Victoria, Australia

editorial

by DON E. FRANCKE

Investigation on the High Cost of Drugs

A Study in Particularism

► IT IS NOT A DIFFICULT TASK to marshal sets of carefully selected facts and figures and to use them to condemn almost any institution of society. People have always done this and will continue to do it whether they are attacking the state, the church, hospitals, the Boy Scouts, or the pharmaceutical industry. The currently popular whipping-boy is, of course, the pharmaceutical industry which is now being subjected to the flagellations of particularism. This is a device whereby an opponent selects facts which, separated from the whole, may contain an element of truth but when related to the whole lead to an entirely different conclusion. Or it may consist of presenting distorted, incomplete, part-truths which imply an onerous guilt.

However, to condemn its critics is not to imply agreement with all practices of the pharmaceutical industry. Like all institutions operated by man, the pharmaceutical industry is subject to human error in judgment and it mirrors to a large extent the morality of the business society in which it operates.

What is objected to in the current investigations are the incomplete and distorted figures, the use of part-truths and the general implication that the pharmaceutical industry is run by groups of avaricious, greedy and selfish groups who are without feeling for the public good.

What pharmacists must recognize and accept is that a distorted picture of the pharmaceutical industry is now being painted. Taken individually and as a group, the pharmaceutical industry represents one of the most responsible, progressive, and fair-dealing institutions in America. While as an industry it is interested in producing profits, at the same time it also performs outstanding service for the public weal. To ignore the contributions of the pharmaceutical industry and to condemn it, or even an individual company, through the use of isolated figures taken out of context or through the emphasis of a few selected considerations is not a method conducive to the attainment of truth.

Drug prices, like those of all commodities, are relatively high in America. But they are not, as a whole, high in proportion to the cost of other goods or in proportion to their costs of development, production and distribution. To arrive at a true figure, the costs of all of a company's products, and hence contributions to patient welfare, must be considered. It is probably true that almost all companies realize a significant profit on a few products. But it is also true that the same companies produce drugs which scarcely pay their way and still are essential for good patient care. The latter could not be produced and distributed without the capital furnished by the former. It does not "pay," for example, for a hospital to have an artificial kidney available—but more and more hospitals provide this service because it is essential for good patient care. In the same manner it does not "pay" to develop and produce certain drugs, or to give certain services, because the potential market is too small. But, to the credit of the pharmaceutical industry, these drugs are produced and marketed and these services are made available.

Despite the unfair accusations, it is quite possible that the Kefauver hearings may have a salutary effect on the pharmaceutical industry. Painful as it may sometimes be, it is proper that all institutions be forced to periodically review their objectives and methods. Other American industries have undergone close scrutiny by Congressional committees and have continued to wax strong. Certainly we see no reason why the pharmaceutical industry will be weakened as a result of these inquiries—in fact, the results could very well be the opposite. If it is permanently harmed it will prove a much weaker industry than it appears.

In a few months the complete record of the Kefauver hearings will be available for study and evaluation. Meanwhile, pharmacists should reserve judgment of the accusations hurled at the pharmaceutical industry and, at the same time, should not be too apologetic about drug prices. As professionals supplying an essential service to the public, pharmacists, too, are entitled to a reasonable return for their effort.

After Senator Kefauver has had his say, one may question whether his relatively brief hearings will do pharmacy the damage that is being done daily, year in and year out, by that segment of pharmacy's practitioners who advertise prescription legend drugs to the public at unrealistic prices and engage in other practices which undermine the profession. These are the things with which pharmacy must be concerned. Time will take care of the Kefauver hearings.


the
social
psychology
of
prescription
writing
Vasocort
Spraypak

by NORMAN G. HAWKINS and ESTHER J. W. HALL

► MOST MAJOR PHARMACEUTICAL COMPANIES NOW IN existence have contributed to, and been conditioned by, some interesting technical developments. In 1945 the total volume of prescription business in the United States was less than half a billion dollars, whereas in 1958 it had surpassed two and one half billion. The difference is accounted for in part by shifting of the medical base of operations. In 1900 few specific and reliable remedies were known and those available were chiefly botanicals such as laudanum and digitalis, biologicals or cod liver oil. Only small changes had occurred by 1945, chiefly in the categories of sulfa drugs and vitamins. Today synthetic preparations and new syntheses of the basic synthetics are dominating both medical practice and public imagination.

From 1948 to 1959 new drug distributors sprouted rapidly, while older ones made huge sums which sometimes vanished almost as quickly. The finest index of that period is found in antibiotics manufacture. This class of drugs increased nearly thirteen times in volume, from 240,000 to 3,081,000 pounds, in eight years.[1] Profits from antibiotics were increased from about 35 percent higher to nearly double the average for American business,[2] but the variability of returns was illustrated by ranges among the three leading manufacturers of 5.2 percent to 57.6 percent profit, 37.1 percent to 101.2 percent profit, and 2.3 percent *loss* to 22.2 percent profit.[3] Uncertainty was also exhibited in the fact that 2 of an original 10 varieties were discontinued, 7 appeared and fell into disuse, and 21 others were on the market, in that brief span of time.[4]

Alterations in Medical Thinking

Another factor has been a profound alteration in medical thinking such that prescribing is part of general medical planning, with emphasis on selective and combinational properties of pharmaceutical preparations in relation to prevention, diagnosis, therapy, and research. The physician is no longer concerned with compounding or handling pharmaceuticals, but leaves that to others and concentrates upon assessment and utilization. Furthermore there has been a tendency for pharmaceutical development to reinforce the distinctions among medical specialties, to cater to special interests like the geriatric market, and to operate in various other ways quite apart from the concerns of individual practice.

Great changes have affected the development and character of the modern pharmaceutical industry. Modern medicine is characterized by narrow and multiple specialization, by the devotion of a large amount of time to consultative activity, and by great dependence of the physician upon a communication network including the research laboratory, the specialized professional literature, personal contacts with medical and paramedical personnel, and a variety of standard references and formularies. Formal medical education is now little more than preparation for translating and interpreting this changing mass of evidence.

Technoculture

The retail pharmaceutical industry has reflected technological changes which have had their influence on the whole economy. The technological changes were markedly accelerated, resulting in transformations of great magnitude, after each of the world wars. In the earlier period, chain enterprises, multiple displays in one store, and synthetic and luxury items became for the first time dominant characteristics of trade. The later changes included preprocessing, automation, integrated shopping centers, added services and conveniences. The pharmacy went along with the current. The chain drug-department stores, promoting gadgets and cosmetics, became an American landmark between the wars. But during these years and since, due to the growing complexity of medicine and the rise of white collar crime, society imposed very stringent controls on therapeutic products. The stream of antibiotics, antihistamines, tranquilizers, and the other wonders which pour from the modern chemical laboratory is almost completely under the control of disinterested professionals, due to powerful institutional and legal pressures.

Automation is one aspect of what is coming to be known as technoculture in order to distinguish it from the mechanical and chemical process which has been known for so long as technology. Technoculture has to do with managerialism, or the growth and specialization of a group dedicated to the sole task of keeping things going. They are the people behind, around, and beyond the assembly line who are dedicated to such jobs as the maintenance of efficiency, control of quality, assurance of reputation and prediction of future trends. As the importance of any given segment of any

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Paper presented to the Section on Pharmacy, American Association for the Advancement of Science, Chicago, December 28, 1959.

technoculture increases, the personnel occupying that segment come to have greater authority and influence, various marks of certification and prestige, a jargon of their own, and various elaborations and refinements of their work life which they unconsciously develop in order to mark themselves as a distinct group.

The vast array of pharmaceutical products available, many differing only slightly in their effects, as well as the rapid changes in market conditions and zooming costs, have forced the majority of physicians out of the role of dispenser except where the preparation is an intimate part of their own ministrations to the sick. The individual compounder in turn is incapable of the degree of automation and quality control exhibited by the pharmaceutical factories and the time required for adequate merchandising, and management of a vastly expanded and highly technical prescription business has restricted the retail pharmacist function to that of stocking and dispensing according to medical demand. The medical sales representative or detailman has been freed from many of the less dignified aspects of selling but, on the other hand, is required to have a considerably greater understanding of medical practice, medical terminology, and the problems of pharmacy operations. Each of the parties to the pharmaceutical transaction is now required to have a better grasp on the total situation and to exhibit a greater spirit of mutuality in order to attain his own end.

Unique Economy

It would be interesting to see how the leading schools of economics anywhere between Mills and Marx would fit modern pharmaceutical distribution into their scheme of things. The chief actors in this economy—physician, detailman, pharmacist, and manufacturer—find it almost impossible to compete either singly or jointly for the consumer's dollar. Direct consumer demand is not sought and, in some respects, it is considered undesirable. Medicine is not a commodity in the traditional sense, even though average costs may be computed along with the cost of food, clothing, shelter and utilities. Such terms as "supply" and "demand," "wages" and "capital" are useful in the practice of accounting, but as theoretical concepts for explaining the ethical pharmaceutical economy they are of limited value. It is questionable whether drug usage is subject to the same cyclical pressures and the prestige factors (*e.g.*, conspicuous consumption) as commodities in general.

One might note in this connection, that transcultural economic comparisons have missed a distinctive feature of American pharmaceutical development. In no other nation is there such widely diffused, highly varied and rapidly upgraded distribution of pharmaceuticals to individual purchasers. Yet all this has occurred under a system of remarkably tight regulation. This control, futhermore, is wholly nonpolitical and defies any interpretation of class interest. As a final paradox, this arbitrary, indirect, impersonal system of distribution caters to the individual in an astounding fashion. Pharmaceutical houses have been known to develop pediatric, hypo-allergenic, and other specialized forms of a preparation which are predictably unprofitable, in spite of the fact that such altruism cannot be compensated by good will of the person benefited.

The subtlety and indirectness of American pharmaceutical distribution has called for intensified efforts at legal control. One reason for this has been pointed out by Vorhes.[5] In spite of the supposedly greater rationality and sophistication of civilized man, he still reacts much as his distant forebears did. He is capable of bargaining and will pursue his own best interest when he is face to face with a single distinct seller and a tangible familiar piece of goods, but he is incapable of exhibiting rational control over a complicated system of distribution dealing with intangible properties and services. Another reason is that the federal service recently recognized the need for specialization in this scheme of things. Within a period of three to five years, the group of men policing the distribution of pharmaceuticals under federal statute was almost completely revolutionized. An understanding of medical practice is no longer important, but successful candidates must have a thorough understanding of legal technicalities and a sharp sense for the gathering of evidence. The pressure of these new men of prestige has been felt first by retail pharmacists and editors of publications and, through them, by the entire distribution team.

Hospital Controls

Group controls are of different kinds. In the modern hospital, for example, the individual physician's judgement is theoretically paramount, but anarchy must be somehow avoided. The sacred conception of doctor-patient relations has been modified by demands of physicians themselves for standardization, teamwork, and efficiency. These are necessities in a complex large-scale enterprise, but if the pharmacy is to conform to the pattern it can neither stock small quantities of every conceivable drug nor purchase locally according to request. The chief pharmacist usually has considerable latitude in the enforcement of the hospital formulary, and he may not exercise that discretion. He also controls to a considerable degree the distribution of samples and drug literature. The efficiency promoted through these controls may at times be dissipated in other ways, as when the physician orders grains and the nurse receives grams, or trypsin is labeled Parenzyme without designating the equivalence.

Detailing

In addition to advertising and publishing clinical data, pharmaceutical houses use various other means of promoting their products. Among these are the

sponsoring of scientific symposia, preparing useful educational materials for medical schools, and supplying samples both for research and personal use. Some firms provide medical scholarships, and there is considerable underwriting of refresher courses, gifts of personal or educational equipment, and so on.

These measures are not enough in a rapidly changing, hazardous business. Pharmaceutical manufacture presents the paradox of a relatively stable population in which "demand" is highly unstable and may, on occasion, be totally unrelated to the qualities of the product or the need for it. There is a constant race between innovation and obsolescence, and out of several hundred new products each year only 8 percent are profitable and less than 20 percent repay development costs.[6] It is vital that the few outstanding discoveries be promptly brought to attention, thoroughly explained, and continuously promoted so as to be profitable in spite of price competition from imitators.

The regular personal contact necessary to meet this need is provided by the medical service representative, or detailman. His promotional functions are: describing products in clear and simple fashion; setting forth the indications for use and all known contraindications; listing possible problems or adverse effects and how to avoid them; and accurately explaining dosages.[7]

There are numerous instances in which face-to-face contact is desirable to the physician or the pharmacist. The use of specific and potent remedies in large numbers and varieties and the very frequent duplication or apparent duplication between competing products, as well as the increased opportunities for incompatibility problems, all raise questions which cannot be put to a printed page. Making an official inquiry is time-consuming and it is well established that effective communication cannot always be achieved by means of the written word. Futhermore, a question may be in the back of a physician's mind and not come to the surface except through the stimulation of conversational question and answer. Verbal contact is something with which the physician, particularly, is familiar and at ease in his daily contact with his colleagues and other members of the medical team.

In addition, some of the most useful practical research is what has often been referred to as "bird-dogging." A person who is in daily contact with physicians and pharmacists can, if properly selected and trained, act as carrier for a considerable and profitable amount of clinical knowledge, practical insight, and useful speculation, gossip or rumor. It is becoming increasingly clear that the man who can effectively perform these various functions must have an adequate scientific and professional background, solid indoctrination into the pharmaceutical industry and the place of his company therein, a good understanding of the needs of the medical profession, and the capacity to exercise a high level of discretion, tact, and resourceful ingenuity. Only to such a person will the medical and pharmaceutical professions communicate with sufficient honesty and completeness to make him an effective representative.

In carrying on his work, the detailman must be conscious of the saying among newsmen, "You've got to have a peg to hang your story on." It is the rapid proliferation of "pegs"—new products, new applications, and new results—that serves to produce for him both opportunities and challenges in this task. He has a limited time in which to make the most of his opportunity, usually between 5 and 11 minutes. He must plan carefully how much to devote to each item or application and in which sequence to bring out the various features to best advantage.

The detailman does not operate in a vacuum. His clients cannot discuss a complete unknown, also they will see no point in covering matters which ought to appear in permanent printed form. Ideally, his company will have made use of certain motivational technics. One technic is timing announcements to coincide with important findings by scientific investigators. Another is to make advertising conform as nearly as possible to the format and theme of outstanding journals. A third is to vary the wording of advertising so as to emphasize for various interest groups, a particular point lying nearest their goals and aspirations. Timing promotion to "hit" seasonal demand would be still another.

Reputation of Company

The detailman also utilizes the reputation of his company. This principle is frequently denied by detailmen as well as by their clients, nevertheless it applies in many ways. The office nurse or receptionist definitely responds to this institutional stereotype. The extent to which it influences the makeup of hospital formularies is problematical, but many chief pharmacists and medical administrators have decided biases and it is human nature to be influenced by these biases. Even physicians who have already denied in an interview that they have any choice among companies can be induced to reveal that their choices of long established competitive preparations are dominated by one or two companies, and that they associate one or two company names with important new discoveries in a number of unrelated areas, sometimes quite contrary to the facts.

That pharmaceutical manufacturers believe in the importance of reputation is evident in their conduct. They try to perform services which please, impress and disarm the medical profession. They associate their names with such prestige symbols as ethical principles, unselfish research, encouragement of education, and promptness both in drug development and professional service. It would be interesting, though possibly quite difficult, to discover the extent to which these activities are related to generic transfer. This phenomenon, in

which a trade name is substituted for the definitive name of a whole class of products, has been noted many times in general merchandising. Examples are Jell-O, Frigidaire, and IBM. Sometimes the effect can be traced to euphony, priority, patentability, or agressive financial operations. The distinction of proprietary from generic names has long been a source of pride in medicine, but it is now widely admitted that generic transfer is occurring. Not only interns, but also general practitioners, occasionally even specialists, attach the name of one company's product to an entire new group of synthetic drugs.

Every detailman strives for something approaching a generic transfer in the collective mind of the prescribers and dispensers of his products. Unfortunately, there is no good evidence that the factors which bring this about in connection with ordinary merchandise are equally valid in the pharmaceutical setting. The factor of priority, for example, can even be unfavorable. Everyone who has been in practice since 1949 can remember the dramatic surge toward leadership and equally dramatic blight of an antibiotic which produced blood dyscrasias. By the time this appears in print, various cases of jaundice resulting from prescribed usage may have wrecked a very promising tranquilizer. Psychotic episodes are causing a slowdown in the distribution of a number of drugs. The general air of caution and cynicism is intensified by authoritative claims that much more damage goes unnoticed than is brought to the attention of the medical profession.

The arrangement for prescription drug distribution in the United States is so foreign to the common stereotype of economic activity it is occasionally misunderstood by western European contemporaries. Recently a distinguished British medical journal discussed the phenomenal growth of detailing as a campaign to stimulate direct buying by physicians.[8] Not only are the economic and social relations distorted by this connotation, but it also overlooks the numerous institutional services and "medical partnership" activities of major companies.

Influence and Diffusion

Such a highly organized, unusual, and economically important activity as prescribing drugs has naturally attracted considerable attention. Various investigators have sought to find what leads to adoption of a noncompetitive innovation or one of several competitive offerings, continuing to use one preparation rather than trying others, using many varieties of one class while neglecting another class of products, criticizing or praising the pharmaceutical industry, and so on. The sources of influence include journal articles, detailmen, journal advertising, direct mail, medical opinion leaders, pharmacists, professional meetings, and hospital staff discussions.

Research to date represents numerous limitations. The influencing of pharmacists has received little attention, and no published research has dealt with hospital chief pharmacists, a small group controlling nearly a third of the prescription market.[9] Studies of physicians present problems of comparability, inasmuch as direct mail and detailmen reach all physicians, while journal distribution may overlap on some doctors and miss others, and opinion leaders are likely to be sought out rather than seeking the person to be influenced. Studies of recall are difficult: readership can be measured and specific advertisements can be tested for effectiveness, but acceptance of detailmen and the impressions retained from their varied presentations are thorny questions.

The psychological concept of reference-group behavior has been repeatedly discussed in relation to what the physician reports about influences upon his drug adoptions.[10] He tends to think of himself as one of a superior group acting upon factual information and able to critically analyze whatever is represented as factual. Whenever answering questions about his real behavior he is likely to say what his colleagues, if present, would expect him to say in order to perpetuate that stereotype. It is not scientific for a physician to be influenced by brand names, people he likes, companies mentioned by his superiors during medical training, or the experience of his family and friends during illness. Most of all, he should not be swayed by the wishes of patients or the convenience of a company's "recipe" for treatment. He is expected to choose in relation to effectiveness, lack of side effect, ease of administration, and other such scientific criteria.

Whether an interviewee would respond in terms of this social self or in terms of a much-harried individual coping with a highly competitive and rapidly changing business would probably vary according to the interviewer. A detailman attempting the job would almost certainly get information differing greatly from that given a social scientist. The latter, in turn, could not expect the same results as someone identified as a patient, a newspaper correspondent, or a Christian Scientist. The senior author has had some experience representing himself as a sociologist and again as a health scientist, and the latter role appeared to elicit greater spontaneity and frankness. This hypothesis would square with what is believed and taught about the nature of in-groups and out-groups. Oddly enough, even in those studies conducted by organized research agencies, medical sponsorship has apparently not been sought in order to capitalize on in-group attitudes.

Among the sources of influence to which physicians may turn, and still retain their scientific pose, are journals with a scholarly reputation, official meetings, and colleagues either as consultants or as staff conference participants. The consultant role has attracted attention in terms of opinion leaders and their relation-

ship to in-group structure and function. The outstanding study along this line is the one by Menzel and Katz.[11] Their chief conclusion was that a drug innovation is diffused through the medical community in stages corresponding to the extent of social interaction among opinion leaders and followers.

This conclusion has been attacked on the grounds that the reported data did not indicate a high proportion of adoption by those in contact with leaders who did adopt, and that since nearly half the drug sales occur in areas of minimum social contact the idea has limited generality.[12] The opinion leader hypothesis has not been supported by other studies. Only one of five new drugs showed anything comparable to that pattern in the Fond du Lac study;[13] that was a specialty item on which the specialist tied with the detailman as a decisive influence among adopters.

One very important feature of the opinion leader hypothesis is the need for some means of verification other than verbal report, otherwise this verbal evidence may be classed as an example of reference-group behavior. Projective technics were used in a study by Dichter,[14] which showed results consistent with the idea that doctors say what they think colleagues would expect them to. Valuable evidence might be gained by comparing a large group practice with an equal number of individual physicians, or hospital prescribing and office prescribing by the same sample. Indirect evidence may be gained by questioning detailmen and pharmacists on their conception of how physicians make these decisions.

Conclusion

Within a period of less than one generation the marketing of drugs has been transformed. Synthetic drugs developed since 1945 now dominate a prescription market which has expanded more than five times. Compounds are more complex, more potentially hazardous, and subject to a very high rate of innovation and obsolescence. The preservation of huge capital investments hinges upon a small percentage of new products which capture and hold leadership in the face of swarms of imitators.

Analysis of the behavior of this market must start from the premise that the physician, his attitudes and habits, are more important than a knowledge of the products, their distributors and handlers, or the eventual consumer—the patient. In pursuing the analysis, one finds that customary consumer appeals are ineffective, partly because of the sharp division of labor made necessary by technological conditions, and partly because of the pervasive indirectness of the appeal. For these reasons, the study of this market is much less a matter of economics than of social psychology.

Research on prescription drug distribution would be directed toward a unique aspect of American economic and social life. Dynamic technology, merchandising shrewdness, and professional integrity—outstanding attributes of our present economy—are seen as a remarkable composite in this industry. The chief theoretical issue lies in the apparent contradiction between opinion leadership and reference-group behavior among physicians. Considerable challenges are presented in the realm of research design and statistical treatment relating to this market. This line of inquiry may throw considerable light upon general principles of opinion formation, motivation, prestige, and decision-making. The area of study is one which stands to gain rather than lose importance due to the increasing volume and potency of drugs, the trend of specialization, and the gradually rising public expectation concerning medical care.

In view of the financial and manpower impact of the prescription drug market, as well as the presently growing importance of health as a subject for basic and applied research, one might expect an abundant literature on this subject. It would seem to be a matter at least as important for the general public as that of the administration of psychiatric hospitals. Its ramifications are many and its implications for social and economic theory are profound. Yet, what seems to have been produced so far is inadequate economics and not much light on pharmacology. Adequate research may soon be needed as a basis for policy decisions concerning the handling of potentially hazardous drugs.

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FROM MATERIA MEDICA TO PHARMACOLOGY

by Ralph W. Morris *and* Allan M. Burkman

► THIRTY YEARS AGO THE STUDY OF DRUGS WAS ON the verge of maturing from the vagueness of materia medica to the precision of a basic medical science—pharmacology. Today pharmacology is in the process of emerging from the tight therapeutic cocoon of the medical school into the broad expanses of the health professions in general. To what this emergence is due and of what significance this pharmacologic emergence has to the practice of modern pharmacy, especially hospital pharmacy, will be the concern of this first of a series of articles on current topics in pharmacology.

Materia medica—the study of the sources, the descriptions and the preparations of drugs—has for many years held a prominent position in the practice of medicine. However, with the development of chemistry, particularly analytical and organic, the isolation, purification and synthesis of the active ingredients of medicinal plants became possible. Occurring almost simultaneously with the advancements in the physical and chemical sciences were vast technical improvements made in the biological sciences, *thereby enabling* more specific and accurate medical diagnoses to be made. As the result of these improved procedures large numbers of treatable diseases were discovered which in turn precipitated the production of a large number of therapeutic agents each of which had to be evaluated on an individual basis by the hospital pharmacist, either directly or indirectly *via* his committee or consultant activities.

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Increasing Responsibility of Hospital Pharmacist

This multiplicity of diseases and drugs has precipitated an urgent need within the health professions for an up-to-date knowledge of the mechanisms and sites of therapeutic and toxic actions of drugs. For many years physicians attempted to fill this need on the

strength of their personal experiences. However, it soon became apparent that the lack of time and the lack of a thorough training in all aspects of drugs prevented the physician from keeping abreast of the rapid advances being made in pharmacology. Consequently the era has dawned when the only member of the health professions with a thorough academic and practical knowledge of all aspects of drugs—chemical, physical, medical and pharmacologic—and therefore in a position to properly evaluate the merits and dismerits of therapeutic agents is the pharmacist. General practitioners have been slow to make this professional concession; however, hospital administrators and staffs have demonstrated wise judgment by placing hospital pharmacists on their therapeutic or formulary committees, often times as chairman. Therefore, it is now the responsibility of the hospital pharmacist to keep abreast of the newest developments so as to be well qualified to give accurate, personal evaluations on drug actions, whether the inquiry comes from a staff physician or from action of the hospital formulary committee. This then is the increasing role and responsibility of the hospital pharmacist today.

Scope of Pharmacology

In the short span of one generation materia medica has almost been completely supplanted by the science of pharmacology (from the Greek *pharmakon* meaning drugs and *logos* meaning knowledge of), very generally defined as the study of the actions of drugs on tissues. More specifically, however, we must define pharmacology in terms of actions (pharmacodynamic, pharmacotherapeutic, and toxic) and in terms of posology (dose *versus* response). Pharmacodynamics is the study of the actions of drugs on normal living tissues, whereas pharmacotherapeutics is the study of the actions of drugs on diseased living tissues. Toxicology is the study of the actions of drugs as poisons and posology the relation of drug action to their dosage. With this then as the scope of pharmacology, it is not difficult to appreciate the enormous volume of pharmacologic research now emerging from nearly every area within the health professions in addition to the original source—medicine.

It is the intention and hope of the authors that this series of Current Topics in Pharmacology will provide the hospital pharmacist with a brief yet up-to-date discussion of the mechanisms and sites of therapeutic and toxic actions of drugs and in this way facilitate and improve his services to the hospital, the community and the profession of pharmacy.

Factors Modifying Drug Actions

The examination, interpretation and evaluation of both empirical observation and rigidly controlled investigation have provided the pharmacologist with what we may call general *principles* of drug action. We recognize drugs to be chemical entities capable of reacting with substances that form a structural or functional part of the living organism and thereby producing some effect. These principles include theoretic and factual information relating to analyses of selectivities, mechanism and site of action, characteristics of distribution and fate of drugs, as well as those factors that are likely to alter a drug's action.

For the successful use of a therapeutic agent, one must be familiar with many of these principles. It is well known that the action of drugs (*e.g.*, rapidity of onset, intensity and duration of action) may be strongly influenced by a number of factors such as

1. Route of administration
2. Amount administered (dosage)
3. Age and weight of patient
4. Sex of patient

There are admittedly many other elements that can modify drug action. These four, however, are among the most familiar and represent those given the most attention when considering a drug's calculated effect.

Route of Administration

Probably the most important single factor is the route of administration. As to which route is selected, the choice is determined largely by

1. Physico-chemical nature of the drug
2. Site of action desired
3. Rapidity with which a response is desired

A number of methods by which drugs are introduced into the body are presented in Table 1, along with some characteristic advantages and disadvantages.

Dosage

The amount of drug administered (or dosage) is certainly an obvious factor influencing drug action. Details regarding the relationships of dose to effect, however, are not quite so obvious nor are they readily explainable. Through experience we recognize that drug effects can be modified quantitatively and often qualitatively by varying the dose. If we were to administer a drug in increasing concentration to a living system and measure one specific effect of the drug we would find that there exists a range of low doses that will elicit no response. These doses are *sub-threshold*. The lowest dose that will elicit a measurable response is known as the Minimum Threshold Dose (MTD). Increasing the dose beyond this point produces increased intensity of response up to a maximum. No further increase in response is produced by increasing the dose. We have reached the Maximum Effective Dose (MED). Between the MTD and MED, response varies with dose. Here, then, we can control the degree

TABLE I. ROUTES OF ADMINISTRATION

Route	Some Advantages	Some Disadvantages
Oral (P.O.)	Uncomplicated and convenient; involves only the act of swallowing; absorption can be varied using different dosage forms.	Acid reaction of stomach or gastrointestinal enzymes may hasten destruction of drug; absorption may be undesirably slow; some drugs are not absorbed to any significant extent, thus systemic effects are not produced.
Rectal	Nauseant drugs can be given in preference to oral; drugs can be given to unconscious patients or small children who will not take oral medication.	Rate of absorption not always predictable; more rapid than oral for some drugs, less for others.
Sublingual (under tongue)	Very rapid effects elicited with some drugs (*e.g.* nitroglycerin); drug absorbed directly through mucosa of mouth and not affected by presence of food in stomach, pH, or gastrointestinal enzymes.	All drugs are not readily absorbed from this site; irritant drugs cannot be given.
Subcutaneous (hypodermic, S.C.)	Rate of absorption generally faster than oral; more certain that all of a given dose will be absorbed into general circulation.	Sterile drug and equipment necessary; irritating substances may be given but will cause pain and necrosis.
Hypodermoclysis (a type of S.C. injection)	Large amounts of fluid (usually saline) can be injected into subcutaneous tissues in areas where the tissue is thick and loose (*e.g.* thighs, buttocks) Hyaluronidase often incorporated in solutions to aid in "spread" and absorption of fluid.	Use limited to special circumstances requiring infusion of large volumes (*e.g.* replacement of water and electrolytes).
Implantation (a type of S.C. injection)	Solid pellets placed under skin in a form that allows for slow sustained release of medication usually over a period of months.	Use limited to special circumstances (*e.g.* hormone therapy).
Intracutaneous	Useful for local reactions (*e.g.* immunization and sensitivity testing).	Systemic effects usually cannot be obtained; only very small amounts of fluid can be injected.
Intramuscular (I.M.)	Similar to S.C.; rate of absorption can be retarded by using suspensions of poorly soluble forms of the drug or by incorporating the drug in a fatty or waxy medium; rate of absorption usually faster than S.C.	Similar to subcutaneous. Irritant substances are usually to be avoided although they produce somewhat less pain than when given S.C.; injecting into a vein is a danger.
Intraperitoneal (into peritoneal cavity, I.P.)	The drug being exposed to a very large surface for absorption rapidly enters the blood stream; absorption is more rapid than S.C. or I. M. Comparatively large volumes can be given.	Painful; great danger of infection; good chance of puncturing intestine and injecting drug into lumen of gut.
Intravenous (I.V.)	A most efficient route; effects elicited most rapidly; irritating substances, since they are rapidly diluted by blood, can be given; large volumes can be administered.	One of the most dangerous routes since effects are immediate; repeated injection inconvenient particularly in obese persons; danger of missing vein.
Intrathecal (spinal)	Effects are very rapid (as I.V.); particularly useful for drugs affecting central nervous system (*e.g.* local anesthetics).	Experienced, skilled person required to administer drug by this route; use limited to special circumstances.
Inhalation	Rapid absorption due to enormous lung area exposed for absorption.	Limited to substances that can be introduced into trachea (volatile liquids, gases, some nonvolatile solids).
Topical	Direct application to site requiring treatment. Usually for local effect only although some drugs are quite well absorbed through skin.	Systemic effects generally poor.

of response by controlling the dose. This range between the MTD and MED is often called the Therapeutic Range.

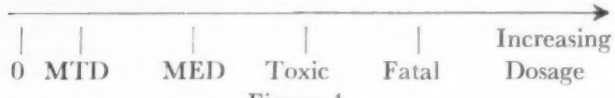

Figure 1.

If we were to continue increasing the dose, a variety of other effects (other than that which we were measuring) would become manifest. These effects might prove detrimental to the life of the animal and hence we are dealing with toxic concentrations of drugs. Eventually a dose would be reached that produces effects completely incompatible with life—a lethal dose (Fig. 1.). With some drugs signs of toxicity are observed at doses below the maximum effective dose level. For such substances the range of dosage that is therapeutically useful may be severely limited (Fig. 2).

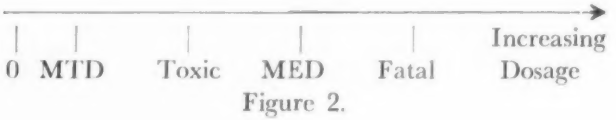

Figure 2.

We occasionally observe that some drugs display qualitatively different effects at different dosage levels. A drug may produce a rise in blood pressure at low doses and yet produce a fall in blood pressure in high doses. Similarly, some drugs will stimulate the central nervous system in comparatively low doses but depress in higher doses. By controlling the concentration of drug, one may produce one of perhaps several qualitatively different responses.

Considerable variation in drug response can be observed among humans and animals that can, in part, be accounted for on the basis of age and weight. The very young and very old (the extremes of age) generally respond in a manner that may differ decidedly from that seen in the young and middle-aged adult. We recognize that metabolic activity varies with age and as a result the biochemical "handling" of a drug will in turn vary. The ability of the body to absorb, degrade, and excrete drugs alters with time.

Age and Weight

The final concentration of a substance depends upon the amount of medium in which it is placed. Although inexactly, the same relationship exists between the dose of a drug and the weight of the individual to which it is given. To elicit a response a given certain concentration of drug must be present at a specific site. The smaller (lighter) the individual, the less the dosage required to provide that necessary concentration. The doses recommended for drugs described in the official compendia are based upon a 70 kilogram man.

There have been a large number of formulas devised to aid the physician and pharmacist in calculating and checking dose requirements for infants and young children. Some of these are based upon age, some upon weight. Among the better known of these formulas are

$$\text{Clark's rule} = \frac{\text{Weight in lbs. X adult dose}}{150}$$

$$\text{Young's rule} = \frac{\text{Age in years X adult dose}}{\text{Age } 12}$$

$$\text{Fried's rule} = \frac{\text{Age in months X adult dose}}{150}$$

It must be emphasized that these rules are rules of thumb that are meant only to aid in approximating doses for children. A considerably more accurate basis for calculating dosage is body surface area rather than age or weight. Although it has been slow in establishing itself as a preferred method, there is no question but that it has distinct advantages over the older rules.

Sex

The predicted response of an organism will frequently depend upon its sex. The obvious anatomic differences between male and female animals are sufficient to explain some varying drug effects (*e.g.*, the oxytocic agents are such only in females). There are, however, less obvious physiological differences between the sexes that result in dissimilar responses to drugs. Women, for instance, are more likely to display the central nervous stimulating action of morphine than are men. And there is the well recognized quantitative difference in drug sensitivity between the sexes. These differences are more easily recognized than explained. One explanation holds that the different hormone ratio in the two sexes is the basis for the observed dissimilarity in response. The hormones, of course, have a very profound effect on metabolism, many phases of which are intimately associated with drug disposition within the body.

Some of these factors that influence drug action can be controlled by the physician (dosage, route of administration); some cannot (age, weight, sex); but all contribute to the drug's response and must be considered in predicting therapeutic efficacy.

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DECOMPOSITION OF PHARMACEUTICAL PREPARATIONS due to chemical changes

by SVEND AAGE SCHOU

► IN THIS SYMPOSIUM WE WILL DISCUSS THE decomposition of medicaments in pharmaceutical preparations, due to chemical changes. As mentioned in the first lecture, stabilization, the means we have at our disposal to control and to limit deterioration, is quite naturally included in this lecture as well.

When decomposition is due to chemical reactions we find that the great majority of the processes can be classified as belonging to one or several of the following well known groups:

Hydrolysis
Oxidation
Racemization
Other chemical decompositions.

The last group being a rather miscellaneous one including processes which do not very well conform to any of the three other groups (e.g. decarboxylation,

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deterioration of hydrcgen peroxide, hypochlorites, formation of a sediment *etc.*).

Hydrolysis

Hydrolysis is one of the destructive processes most frequently occurring in pharmaceutical preparations, since a great many substances are susceptible to hydrolysis, *e.g.*, alkaloids such as the tropa alkaloids, cocaine, physostigmine, several lccal anaesthetics (*e.g.* procaine and amethocaine [=tetracaine]) are all esters. Other alkaloids (*e.g.* ergometrine), local anaesthetics *e.g.* cinchocaine (=cincaine, dibucaine) and barbituric acids are amides, and finally several compounds of a complex structure such as thiamine and chlorphenotane.

The velocity of the processes of hydrolysis depends on the temperature and the *p*H of the solution. As in the case of all other chemical processes, the temperature is of decisive importance for the course of the processes of hydrolysis. The temperature coefficient has in most cases been found to be of a "normal" order of magnitude, *i.e.* 2-3. Thus for the hydrolysis of procaine the temperature coefficient fcr 10° was found to be 3.1 when calculated on the basis of the rate constant at 20° and 37°. A single experiment carried out at 70° C. showed the temperature coefficient to remain unchanged throughout the interval from 20° to 70° C. For the hydrolysis of cinchocaine (Cincain, Percain®) in aqueous solution at the *p*H-value proper of the hydrochloride, the temperature coefficient was found to be 2.54 in experiments at 90° and 100° C. For the hydrolysis of atropine in alkaline medium (dissolved in ethanol containing 0.005 percent water to which had been added anhydrous potassium hydroxide) a Q_{10}° of 1.96 was found. In 1 N hydrochloric acid a Q_{10}° of about 2.2 was found for hyoscyamine.

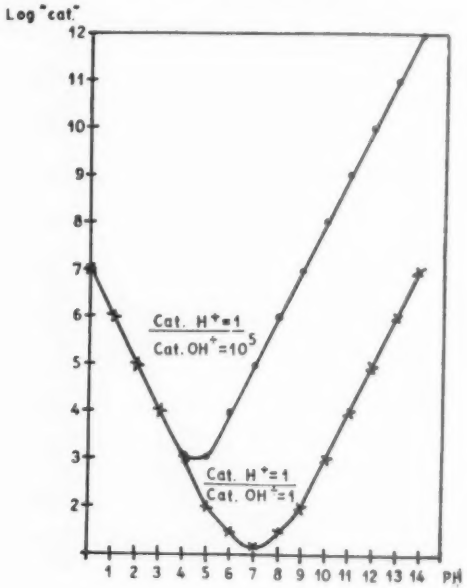
As may be seen from these figures it is possible usually to depend on at least a 100 percent increase in stability if the storage temperature is reduced by 10° C, *e.g.*, if the preparation is kept at, respectively, room temperature and refrigerator temperature.

The most important catalysts in hydrolytic decompositions are the hydrogen ions and the hydroxyl ions, the *p*H thus being a very important factor in determining the rate of hydrolysis and in the stability problem as a whole. The fact that the hydrogen ions as well as the hydroxyl ions have catalytic effects is shown by the occurrence over a certain *p*H range of a minimum of decomposition (or maximum of stability), its position depending upon whether hydrogen ions or hydroxyl ions have the greatest catalytic effect on the process in question.

If the position of the minimum is about *p*H 7 they must be of equal effect. A shift towards the acid side of the scale may be explained by the hydroxyl ions having a stronger catalytic effect than do the hydrogen ions, and *vice versa* in case the minimum has been

Figure 1

Lower curve: *The catalytic action of H+ and OH^- are equal*
Upper curve: *The catalytic action of OH^- is 10^5 time that of H+*
Log "cat.": *Log total catalytic effect*



shifted towards the alkaline side. The former case is the most frequent by far, *e.g.*, in the case of procaine a minimum was found at *p*H 3.6, while for cinchocaine the value is about *p*H 5, for benzocaine 4.9 and for atropine (hyoscyamine) about *p*H 5.

In order that the best possible conditions be obtained for the stability of the preparations an attempt is often made to adjust their *p*H to the value corresponding to the minimum of decomposition. However, in so doing it is necessary to duly consider the fact that the solubility of the compounds often varies considerably with the *p*H, and that often their therapeutic values vary as well, because, among other reasons, the conditions of absorption from the tissue or from the place of application change. Thus it has been judged desirable to use a number of eye drops (physostigmine, atropine etc.) having a *p*H value higher than the one found in aqueous solutions of the normal salt, since the basic form of the alkaloids is considered to be the active one, probably due to their solubility in lipoids. Such medical demands are not easily compatible with the pharmaceutical demands for stability, in addition to which many alkaloids tend to fall out if the reaction of the solution is changed towards the alkaline part of the scale. Hence it is often necessary to compromise, the final *p*H value being a mean between the ideal "pharmaceutical" *p*H value and the ideal "medical" value. The latter may thus have been determined by consideration of the therapeutic effect, but more often it is based on physiological considerations, *i.e.*, the wish to adjust the *p*H of the preparation to that of the tissue in the place of application, the "physiological" *p*H value. Recently it has been shown that a previous application of a drop of sodium borate solution will increase the absorption of certain drugs (*e.g.*, atropine) from eye drops.[1]

The *p*H values of the preparations may be adjusted by means of buffers, and this has been done with success, *e.g.*, in the case of penicillin eye drops. But the *p*H value chosen for reasons of stability often deviates more from the physiological *p*H values than was true in the case of penicillin solutions (*p*H 6.5), it is usually preferred to add free strong acid or base rather than buffers, the buffer capacity proper of the tissues then being sufficient to realize the physiological *p*H when using the preparation.

An adjustment of the *p*H is thus the most simple and the most effective way to stabilize preparations liable to undergo hydrolytic changes.

It should finally be mentioned that it has been found possible to influence the rate of a hydrolysis by adding a "stabilizer" proper. In experiments with procaine it was first demonstrated that an addition of theophylline will reduce the rate constant by a factor of about 3, and the phenomenon has been demonstrated in a few more cases. Whether this is simply due to a complex formed, as I believe, or to an unknown interaction can't be said. The observation is interesting, but has so far had no practical consequense (Higuchi *et al.*[2]).

Oxidation

A destructive process of an importance equal to that of hydrolysis is the oxidative decomposition. This we realize when we consider problems such as the preparation of stable solutions containing adrenaline, noradrenaline or ferrous salts or a problem such as the stability of fats and oils.

A substance is oxidized when it gains electronegative atoms or radicals or loses electropositive atoms, radicals or electrons.

In order to treat the oxidative processes from a more theoretical point of view, an attempt must be made to relate the stability of the preparations, to the general laws applicable to oxidation-reduction systems. However, I should like to point out right away that usually it is not possible to carry out kinetic studies on oxidation processes as such concerning general stability problems, due to the fact that in the case of organic remedies the course of the reaction is too complicated and often determined by several variable factors. On the other hand, the oxidation potential (the redox potential), which is constant and relatively easy to determine, will provide certain information concerning the predicted stability of a certain preparation.

Here as before it is not possible to consider the theoretical background in detail, but for reasons of definition in particular I should like to bring to your attention certain elementary facts. Any pharmacist is familiar with the instability of the ferrous salts, in that they are oxidized to ferric salts, and likewise they are familiar with the reverse process. The ferric ion/-ferrous ion are said to form a redox system consisting of an oxidated form, an ox-form, and the corresponding reduced form, the red-form. If we want to compare the phenomena pertaining to different redox systems, and in particular the outcome when two redox-systems are combined which is in fact the case when one of our preparations deteriorates due to oxidative changes, then the oxidation potentials of the two systems assume a decisive importance. For the sake of simplicty, let us consider the oxidation potential of the system ferric/ferrous, where the process determining the change from the ox-form to the red-form represents the ability of the ferric ion to take up an electron and that of the ferrous ion to give off an electron:

$$Fe^{+++} + e \rightleftarrows Fe^{++}$$

It turns out that in this case it is easy to measure an electric potential between a platinum electrode and the liquid containing the redox systems; it further turns out that this oxidation potential, E, is dependent upon the ratio between the ox-form and the red-form in the following way

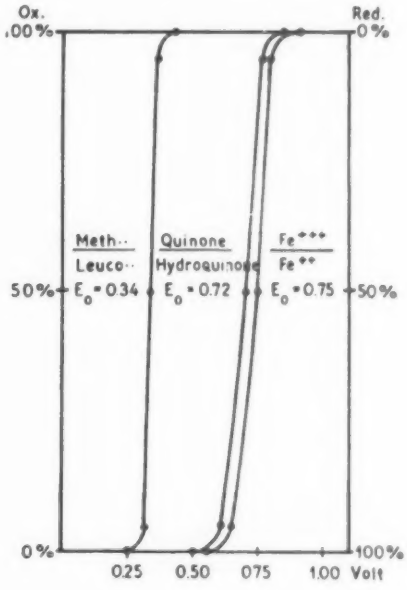
$$E = E_o + \frac{0.06}{n} \log \frac{C_{Fe^{+++}}}{C_{Fe^{++}}}$$

E_o being the so-called normal potential and n the number of electrons taking part in change from the ox-form to the red-form; in our case then n equals 1.

It appears directly from the equation that if $C_{Fe^{+++}}$ is equal to $C_{Fe^{++}}$ and the ratio thus is 1, E becomes equal to E_o, and the oxidation potential measured then equals the normal potential; but that otherwise the oxidation potential varies with the ratio between the concentrations of the two forms within the redox system. This is illustrated in the following figure, where the abcissa represents the three systems, while the ordinate represents percent ox- or red-form.

Figure 2

The oxidation potential as a function of the relation between per cent oxidized form and per cent reduced form



Certain oxidation potentials are dependent upon and others independent of the hydrogen ion concentration of the system. But a common feature of all redox systems is the fact that the higher the content of the oxidizing component (*i.e.*, the ox-form) of the system, the more positive the potential *i.e.*, the more oxidizing power of the solution and the less reducing power, and *vice versa*. However, the oxidation potential is not determined by the absolute concentrations, but by the *ratio* between them. But of course a solution containing higher absolute concentrations of the redox system will ipso facto have a higher oxidative buffer capacity. The higher the value of the E_o, *i.e.*, the oxidation potential, the more strongly oxidizing is the redox system in question. When two redox systems are combined, as is the case with many pharmaceutical problems, the system having the higher oxidation potential oxidizes that having the lower one.

During the course of the process the two potentials approach the same value, and when they are identical an equilibrium is established. In many cases the reactions are encumbered with a certain inertness, and this is the cause of the extreme sensitivity to catalysts commonly found in oxidative processes (*e.g.*, the oxidation of fats).

As mentioned above, it is easy to measure the oxidation potential of a solution electrometrically, but it is even easier to measure it colorimetrically. As in the case of *p*H measurements, where the electrometric determination is the more exact one, but where the information obtained by simple colorimetry is often sufficient, it is possible here to obtain tentative information concerning the oxidation potential of a certain system by using the so-called redox indicators. These indicators are redox systems which change color at certain definite values of their oxidation potential, the two forms being of different colors, or one form is colored and the other one is colorless. But here again we frequently encounter the difficulty of inertness of the reaction, something which is unknown in the case of acid-base systems, and which therefore presents no problem for colorimetric *p*H measurements. Methylene blue may serve as a simple example of a redox indicator. If methylene blue is contained in a solution at a *p*H of 2, the color change occurs between 0.3 and 0.4 volts. If the intensity of the blue color of the solution remains unchanged, the oxidation potential of the solution is above approximately 0.4 volts. It is below about 0.3 volts when the solution is decolorized forming colorless leucomethylene blue; if the solution is only partly decolorized the oxidation potential is between 0.3 and 0.4 volts.

In a system such as the Fe^{+++}/Fe^{++} mentioned here the oxidation potential is independent of the concentration of hydrogen ions, but in many other cases where hydrogen ions take part in the redox reaction the potential is dependent upon the *p*H, mentioned above. This is true in the case of certain acids such as, *e.g.*, ascorbic acid or the many weak acids of pharmaceutical importance such as various phenols (*e.g.*, adrenaline). The system quinone/hydroquinone is a classic example, the reaction (at the electrode) being the following:

$$C_6H_4O_2 + 2H^+ + 2e^- = C_6H_4(OH)_2$$

Here the oxidation potential may be expressed by the following equation

$$E = E_o + \frac{0.06}{2} \log \frac{C_{H}^{2+} \cdot C_{\text{quinone}}}{C_{\text{hydroquinone}}}$$

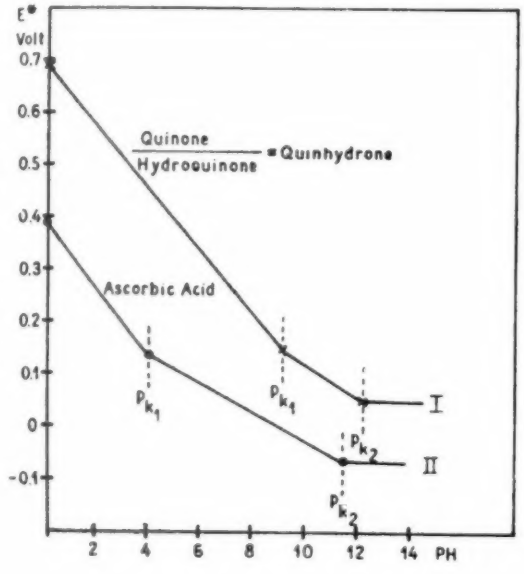
On this reaction is based the previous extensive use of the quinhydrone electrode (in the case of quinhydrone C_{quinone} equals $C_{\text{hydroquinone}}$). It appears from

the equation that an increase in the concentration of hydrogen ions (decreasing *p*H) causes an increase in the value of E. This means that the red-form of the system is less readily oxidized when the *p*H is low. Since now the systems pharmaceutically used usually occur in red-form (adrenaline, noradrenaline, morphine, ascorbic acid, and many others) this means that it is possible—as we all know—to stabilize these compounds by a lowering of the *p*H. This then in many cases becomes the most important procedure usable for the stabilization of pharmaceutical preparations with regard to oxidative changes.

We have already mentioned that in the case of oxidative processes they are often encumbered with

Figure 3

Relation between oxidation potential and pH *



*G. Schill, Farm Rev. *58*, 45 (1959).

an inertness so pronounced that even if the affinity is sufficient no reaction takes place. In such cases the rate of the reaction, and hence apparently the over-all course of the process will depend upon the presence of one or more catalysts. Predominantly the catalysts involved are metal ions, in particular cupric or ferric ions. The type and amount present of the catalyst is of decisive importance, but is usually not known, and as they are present as impurities the course of oxidative processes catalyzed by metal ions is often unpredictable in practice, and hence it is difficult to subject it to kinetic treatment. On the other hand, the method of stabilization is simple in this case, requiring merely the elimination of the catalyst. This has been known for a long time, but has only been systematically explained and practiced in recent years by the use of solvents free from metal ions (glass or quartz distilled water), or by the addition of a compound forming chelates with the metal ions, *e.g.,* tetracemine (Komplexon®, EDTA). In this way the stability of, *inter alia,* adrenaline and morphine solutions has been increased successfully and considerably.

Autoxidations

Many oxidative changes in pharmaceutical preparations, and in particular of fats, have the character of autoxidations.

An autoxidation is an oxidation proceeding slowly under the influence of atmospheric oxygen. Autoxidations are often chain reactions initiated by activation of a molecule thus forming a radical with oxygen and subsequently with another molecule of the compound leading to the formation of another radical which then continues the reaction. Such chain reactions may be recognized by the fact that the rate of autoxidation may be changed radically by the addition of even extremely small amounts of substances of either positive or negative catalytic effect. Often the processes are also autocatalytic, *i.e.,* the oxidation products formed affect the reaction catalytically. Of special interest are negative catalysts, so-called antioxidants, which if they break up the chain during autoxidation are called inhibitors. Strictly speaking they are not proper catalysts since they are actually used during the process. Usually the substances which act as and are used as antioxidants are easily oxidizable compounds such as phenols and amines, but inorganic compounds as, *e.g.,* pyrosulphite may also be used. They act on the principle of a single molecule of antioxidant preventing the progress of the reaction by reacting with one or more of the compounds involved in the chain reaction, and thus impending a long chain of reaction with perhaps several thousand reacting molecules. Not until all of the antioxidant has been used does the oxidation process proper commence, and then frequently at a great rate, *i.e.,* the so-called induction period is finished.

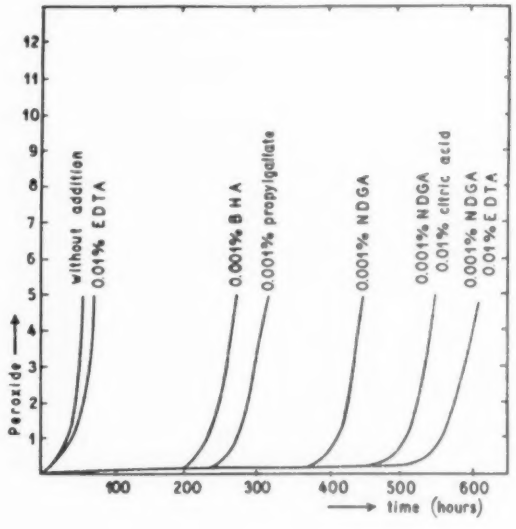
The autoxidations may be divided up into two groups, the reactions of one group causing an uptake of oxygen, while in the other group a dehydrogenation takes place. The fatty substances may serve as an example of the first group, and the phenols as an example of the second group.

The problems of autoxidation and antioxidants have been studied particularly in the case of the fatty substances, since their rancidification is due to autoxidation and is of great economic importance. The process of going rancid is of pharmaceutical interest as well due to the use of the fatty substances as basic substances in ointments and as solvent particularly for the easily oxidizable, lipid soluble vitamins. The reason why most fats, and the vegetable ones in par-

ticular, are fairly stable without the addition of preservatives is their content of natural antioxidants, the most important of which are the tocopherols. Ethereal oils as well are liable to go rancid due to autoxidation processes; this is true in particular of ethereal oils containing high percentages of unsaturated terpenes. When going rancid the fragrance and taste of the ethereal oil is destroyed, and furthermore the rancid oil may cause dermatitis when used on the skin.

Figure 4

*The effect of different stabilizers on the oxidation of oil of terebinth**



Of equal interest is the autoxidation of the phenols, a great many pharmaceutically important substances (morphine, apomorphine, adrenaline, oxedrine, resorcin, etc.) being phenols. Among these the diphenols, particularly those with hydroxy groups in the ortho position, will be especially easily oxidized and hence cause discoloration of preparations in which they are used, the compounds formed being, *e.g.*, polymers of quinoid structure (formation of melanin). These colored decomposition products are often formed only in slight amounts, but due to their vivid colors they are recognizable at an early date and necessitate the rejection of the preparation before it is actually required with respect to the therapeutic effect. The aim has therefore been to find a suitable antioxidant as well as a substance preventing the discoloration of the preparations. A substance more or less combining both of these properties is sodium pyrosulphite, which is used to a considerable extent as an addition to official preparations.

The oxygen concentration is of importance in autoxidation processes, but this is not always considered very thoroughly. In the pharmaceutical literature the term oxygen tension is occasionally used instead, but this is somewhat misleading owing to the fact that the oxygen tension does not vary in a manner parallel to that of the oxygen concentration. Thus the oxygen tension of a liquid is defined as the pressure of oxygen required above the liquid to establish an equilibrium, *i.e.*, indicated as, *e.g.*, mm. Hg, while the concentration is indicated as, *e.g.*, ml. O_2 per liter. When studying the rate of the reaction for an oxidation at different temperatures it is necessary as mentioned above to consider both the direct effect of the temperature and the effect of the temperature on the oxygen content (concentration of oxygen) of the liquid. Thus, if a preparation having a temperature coefficient of 2 for 10° C. for the rate of reaction of its oxidative decomposition is moved from storage at 15° to 5° C., the direct dependence on temperature will cause the rate of the reaction to be reduced to half its initial magnitude; simultaneously however the concentration of oxygen will increase by about 25 percent usually resulting in an increased rate of oxidation. The resulting rate is hence caused to exceed that calculated on the basis of van't Hoff's rule. However, a consideration of the oxygen tension shows this to be unchanged (ignoring the water vapor pressure), the partial pressure of the oxygen in the atmosphere being unchanged. The reason why the concentration of oxygen is only rarely taken into consideration is probably the fact that usually it is not possible to change it enough to affect the stability to any considerable extent. In the case of certain oxidations it is possible to compute stoichiometrically the magnitude of the consumption of oxygen for a 100 percent oxidation; but in the case of chain reactions it is not possible to make a similar calculation; and even if it were possible to calculate the slightness of the oxygen concentration required for the reaction to proceed, the amounts of oxygen involved would turn out to be of an order of magnitude so that it would in practice be extremely complicated, and sometimes outright impossible, to eliminate it from the storage container.

The so-called *synergists* should be mentioned in connection with the use of antioxidants. Strictly speaking synergists do not inhibit the process of oxidation, but they often augment the effect of the antioxidants. The use of synergists has assumed particular importance in the case of stabilization of fats and of fat-soluble vitamins.

It is difficult to relate the effect of the synergists directly to the oxidation potential of the system. But an examination of the different types of synergists reveals their structure to be of such a kind that their effect may very well be explained by a formation of

*After *L. Fryklöf*, Farm. Rev. *53*, 317 (1954).

complexes with metal ions, thus limiting the extent of the catalysis. The following types may be mentioned: acids (citric acid and phosphoric acid), amino acids (α-amino acids such as phenylalanine and tryptophane) and polyvalent alcohols (*e.g.*, glycerol and sorbitol). I should like to add that a more direct participation of the synergists in the reaction mechanism has also been suggested, but as mentioned it would be difficult to explain.

The practical use of synergists in combination with antioxidants offers a very valuable increase of their ability to limit the autoxidation of fats.

The effect of the *temperature* on the processes of oxidation is the same as that on other chemical reactions, and the temperature coefficients are of the same order of magnitude as in the case of the processes of hydrolysis; hence a 100 percent increase in stability may be anticipated if the preparations are kept under refrigeration in the case of substances sensitive to oxidation. However, it is necessary to keep in mind the fact that simultaneous with a reduction of the rate of the reaction the cooling causes also an increased solubility of the oxygen in the liquid. Thus an increased rate of the reaction is obtained, the resulting total reduction of the rate being lower than the calculated one, at least in the case of processes proceeding stoichiometrically. However, since most oxidative decomposition processes are assumed to be chain processes and thus comparatively independent of the oxygen concentration this fact is usually insignificant.

Summarizing our present knowledge of the oxidative processes, the following means of stabilizing pharmaceutical preparations may be said to be at our disposal:

1. *Removal of the oxygen present.* This procedure will in many cases be of value, but the theoretical basis is not at all clear. But when the destructive process is an autoxidation the removal of oxygen is well motivated.
2. *Reduction of the rate of reaction by reducing the temperature.* This procedure is applicable in all cases.
3. *Increase of the oxidation-potential through a decrease of the pH.* This procedure is applicable in cases where the oxidation is due to a transfer of electrons (adrenaline a.s.o.).
4. *Addition of a redox system, more easily oxidized than the system itself* (*e.g.*, the use of antioxidants, stabilization with ascorbic acid, pyrosulphite).
5. *Chain-reactions are prevented or delayed by the addition of inhibitors* (phenols, amides and other antioxidants).
6. *Reduction of the rate of reaction through elimination or through complex-formation of catalysts present* (medium free from metal ions, or addition of complexing agents, EDTA or the like).

Racemization

Racemization is a process in which optically active substances may lose their optical activity without changing their constitution. The racemization processes form an important factor for the stability of pharmaceutical preparations, since a number of optically active compounds are used therapeutically, and since the biological effect of the dextro form (the d-form) is usually different from that of the laevo form (the l-form). Usually the l-form of the optically active substances is the most effective and hence the most frequently used. When studying the stability of preparations containing these substances the procedure is therefore to follow the reduction in optical activity during preparation and storage, and to pronounce the compound to be racemized 100 percent when the optical activity is zero. This does not mean that the therapeutic value is also zero; there is still 50 percent of the l-form left in the preparation, and the d-form formed from the l-form is usually not completely inactive. Thus the process of racemization comes to a standstill, to an equilibrium, when the racemic form containing 50 percent of the l-form and 50 percent of the d-form of the active compound has been formed; this is also the case if the pure d-form is used as the starting material.

Very little is known concerning the causes of the racemization. The rate of the reaction varies a great deal and depends on the temperature, the solvent, and on the presence of light and catalysts—often alkaline compounds, *i.e.*, hydroxyl ions, but hydrogen ions also have a catalytic effect, and thus a *p*H-minimum exists for the reaction. The position of this minimum may, however, vary a great deal over the *p*H scale. Finally, the racemization appears to depend upon the functional group bound to the asymmetric carbon atom, *e.g.*, aromatic groups accelerating the racemization.

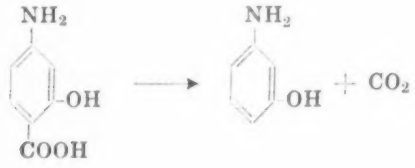
The processes of racemization may be treated in the same way as the other decomposition processes: determination of rate constant, temperature coefficient, and dependence upon the *p*H, and on the basis of these factors establishing of optimum conditions for the preparation and storage.

As to the order of the racemization process it must be, and is found to be, of the first order, and the rate problems are thus easy to handle experimentally and graphically. The Q_{10} has been found to be of the usual order, *e.g.*, of from 2.1 to 3.8, dependent upon the *p*H and the temperature, for adrenaline, noradrenaline and phenylephrine.

A few examples only shall be mentioned of other chemical decompositions.

Decarboxylation

Decarboxylation has been studied due to the pharmaceutical interest in para-aminosalicylic acid (PAS), but kinetic data are not available. The process:



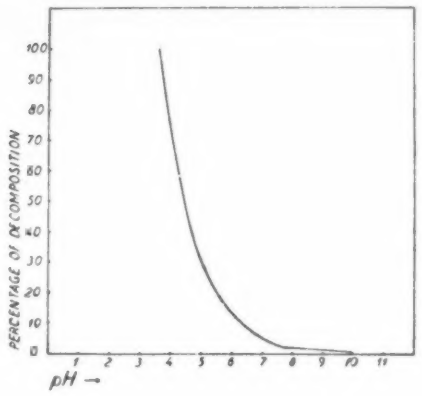
must be of the first order and has been shown to be highly dependent of the *p*H, the decarboxylation being catalyzed by hydrogen ions, as it is seen from the Figure 5 above, right.

It would be tempting to believe, that this process could be controlled through an adequate CO_2-pressure over the solution, as it is known and self evident for solutions of sodium bicarbonate. But this is not the case. The decarboxylation is not a simple reversible process, and the shift in the *p*H is the determining factor. The decarboxylation of para-aminobenzoic acid is also of pharmaceutical interest and is known to take place, but only when the system is treated at an extremely low *p*H and at a high temperature, this molecule being much more stable than the corresponding PAS-compound. No experimental data permitting kinetic considerations are available in this case either.

The decomposition of hydrogen peroxide is another

Figure 5

Decomposition of para-aminosalicylic acid *



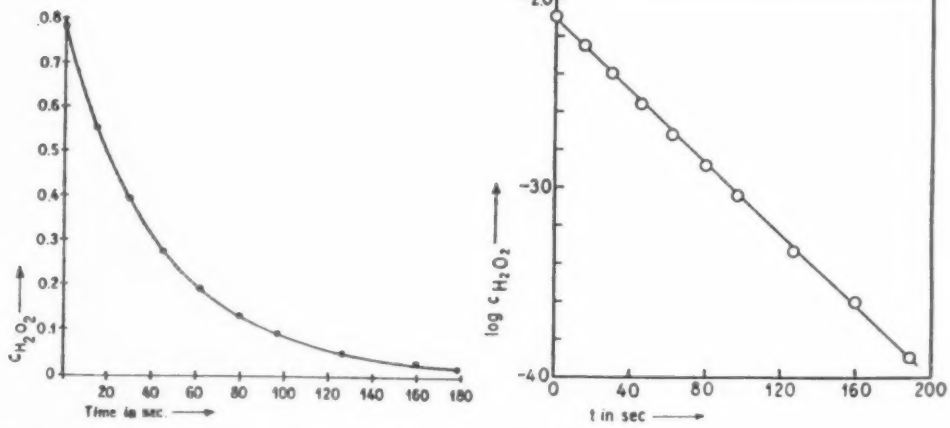
example. This reaction has been known for a long time, and has been studied extensively, the reaction mechanism being complicated and difficult to study, due to the sensitivity to catalysts. A multitude of compounds are known to catalyze the process, *e.g.*, salts of heavy metals, powdered substances, rough surfaces, certain enzymes *etc.* Also several stabilizers, so-called negative catalysts, are known and have been thoroughly tested (acids, acetanilid, phenacetin).

The decomposition of hydrogen peroxide catalysed by the enzyme catalase has been studied kinetically, and the process is of the first order as shown in the two following figures.

*After V. *Gauno Jensen* and *E. Jerslev*, Dansk. T. Farm. *26* 227 (1952)

Figure 6 and 7

Decomposition of hydrogenperoxide catalyzed by catalase *



*After *V. Sten Andersen*, Dansk T. Farm. *30*, 274 (1956)

Figure 8

Decomposition of sodium hypochlorite at different temperatures. Ordinate per cent destruction *

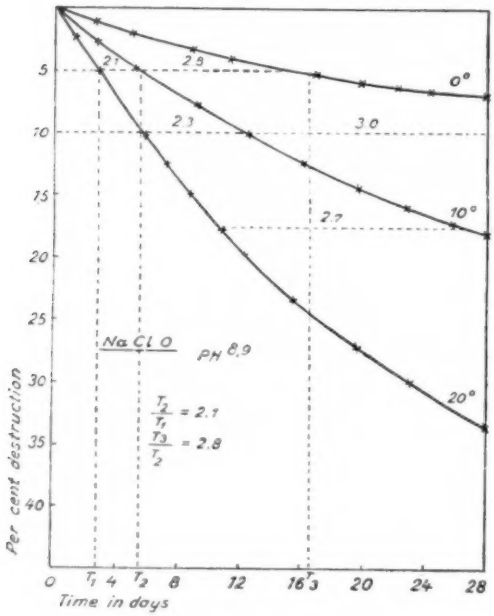
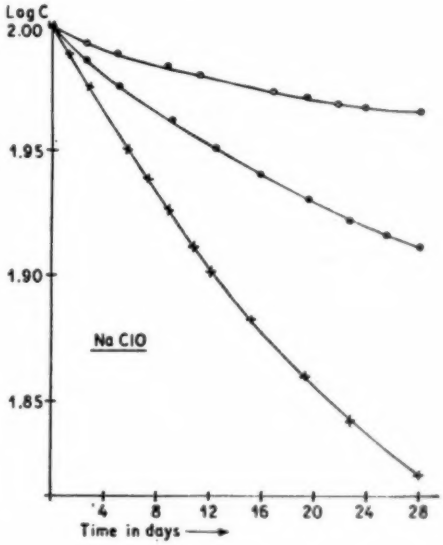


Figure 9

The same experiments as in Figure 8 but the ordinate being the log of the ordinate values in Figure 8



A process such as the decomposition of sodium hypochlorite is highly dependent upon the *p*H in the solution. When stored in solution the hypochlorite is decomposed forming chlorate and chloride, and to a lesser extent, in a competing reaction, chloride and free oxygen. We can use this as an example of the value of plotting the decomposition as a function of time, to obtain information concerning the order of the reaction. The resulting graph (Fig. 8) could very well be that of a process of the first order, but if so, we should get straight lines, when we plot the log c (here the log of the decomposition) against time. The bent curves in figure 9 tell us that the process is not as simple as that.

With these few examples we will leave this vast and heterogeneous group and finally draw the attention to the complication we must often face in the study of the stability problems: that several competing reactions can take place at the same time in our preparations. The sympathomimetic amines, important drugs that they are, are at the same time racemized and oxidized. The ergot alkaloids are racemized, oxidized and hydrolyzed, *etc.*

That this complicates our study is evident, but in handling one process at a time the pharmaecutical research has already obtained useful results.

I do hope I have been able to show you that the decomposition of the pharmaceutical preparations due to chemical changes follows the well established laws of physical chemistry, and so does the stabilization of the preparations. The study of the destructive process thus forms the basis for the study of the stabilization.

A continuous study of the decomposition of the pharmaceutical preparations is in itself a study of the stabilization, and to follow this line is today imperative in the pharmaceutical research.

*After *S. A. Schou*, Dansk T. Farm. *25*, 153 (1951).

Adresse des Autors: Prof. Dr. *S. A. Schou*, Royal Danish School of Pharmacy, Copenhagen, Denmark.

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THE RETROBULBAR INJECTION OF LIDOCAINE (XYLOCAINE) FOR ANESTHESIA

COMPARATIVE STUDY USING 2 PERCENT AND 4 PERCENT SOLUTIONS

by DAVID S. JOHNSON *and* EDWARD SUPERSTINE

► A STUDY WAS UNDERTAKEN TO DETERMINE THE relative advantage of using a 4 percent solution of lidocaine (Xylocaine) hydrochloride over a 2 percent concentration of the local anesthetic agent. The study includes 31 cases in which either the 2 percent or 4 percent solution of lidocaine was used as the injection material.

Procedure

The procedure followed was the same in all cases. Preoperative medication consisted of the use of secobarbital sodium injection 100 mg. (200 mg. in obese and young patients) by the intramuscular route two hours preoperatively. Meperidine hydrochloride was used in conjunction with levallorphan tartrate, 100 mg. and 1 mg. respectively, one hour preoperatively and administered by the intramuscular route. An intramuscular injection of promethazine hydrochloride, 25 mg., was administered one-half hour preoperatively.

The sterile solutions of lidocaine hydrochloride 2 percent and 4 percent were prepared in the Pharmacy Department and their strengths were not known to the surgeon. The solutions were prepared as follows:

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Lidocaine Hydrochloride Injection 2% With Epinephrine 1:100,000 & Hyaluronidase 7.5 U/ml.

Lidocaine Injection 2% with Epinephrine 1:100,000 (Xylocaine with Epinephrine)	20.0 ml.
Hyaluronidase (Wydase)	150.0 TRU

Packaged in 20 ml. sterile rubber stoppered vials.

Lidocaine Hydrochloride Injection 4% With Epinephrine 1:100,000 and Hyaluronidase 7.5 U/ml.

Lidocaine Injection 4% (Xylocaine)	20.0 ml.
Epinephrine Injection 1:1000	0.2 ml.
Hyaluronidase (Wydase)	150.0 TRU

Packaged in 20 ml. sterile rubber stoppered vials.

SEND COPY OF THIS REPORT TO PHARMACY

Lidocaine (Xylocaine) Injection

VIAL #_____

CONTROL #_____

Patient's Name_____
Last First

Case Number_____

Date_____

Time Surgery Is Begun_____

Time Ended_____

Surgeon_____

OBSERVATIONS

1. Amount of injection: 1st____cc. 2nd____cc.
2. Degree of anesthesia at surgery:
3. Duration during surgery:
4. Complications at surgery:
5. When does pain start to return:
6. When is medication necessary, What time after surgery:
7. Amount of reaction from injection:

Table I. Findings After the Use of Lidocaine 2% and 4% Solutions for Retrobulbar Anesthesia

Percent Solution	Degree of Anesthesia[1]	Duration of Analgesia[2]	Amount of Local Reaction
	G	4 hr.	M
	E	3 hr. 30 minutes	N
	E	NM	N
	G	3 hr. 5 minutes	N
	G	4 hr. 15 minutes	N
	F	3 hr. 45 minutes	N
	G	4 hr. 45 minutes	N
4	E	NM	N
	P	NM	N
	E	1 hr. 55 minutes	M
	G	7 hr.	VL
	E	3 hr. 20 minutes	VL
	G	4 hr. 10 minutes	VL
	E	3 hr.	M
	F*	3 hr. 15 minutes	N
	E	3 hr. 5 minutes	VL
	F	NM	N
	E	2 hr. 35 minutes	M
	G	NM	N
	G	NM	N
2	G	NM	N
	E	4 hr. 30 minutes	N
	G	NM	N
	E	4 hr.	N
	E	2 hr.	VL
	G		
	G		
	G	NM	N
	G	NM	N
	G*	9 hr.	N
	F*	4 hr. 30 minutes	N

1. Degree of anesthesia (upon command): P=Poor . . . movement of Recti muscles; F=Fair . . . very slight movement of two of the Recti muscles; G=Good . . . movement of one Rectus muscle; E=Excellent . . . No movement

2. Duration of analgesia: From onset of anesthesia until pain was perceived and medication was required.

*Complications.

The containers were labeled as follows:

Sterile Solution Lidocaine
(Xylocaine) Vial # 107
For Investigational Use Only
Control 011559
Expires January 30, 1959

A total of 10 ml. of the anesthetic solution was administered in the following areas: 1.5 ml. in the inferior retrobulbar area, 0.5 ml. in the superior rectus muscle, 2 ml. in each of the upper and lower lids at the area of the ciliary ganglion, and 4 ml. in the outer canthus. Ten minutes after this injection pressure was applied on the eye for 5 minutes by the clock. Twenty minutes after the injection surgery was begun. The same injection technique was followed in all cases and there were no readministrations.

There were a total of 31 cases in the study. Only the Pharmacy Department had a record of the actual strengths of the various vials of anesthetic mixture. The chart of findings (Table 1.) is divided into 15 cases to whom were administered the 4 percent solution of lidocaine and 16 cases administered the 2 percent solution.

Of the 15 patients receiving the 4 percent solution, 6 showed an excellent response in terms of degree of anesthesia, 6 a good response, 2 a fair response and 1 patient a poor response. There was one complication in this group; the patient was deaf and got up off of the table during a cataract extraction and there was vitreous loss. Three patients in this group required no medication (NM) indicating no preception of pain at any time after the surgical procedure. Of the twelve patients requiring medication, the average time postsurgically at which medication was required was three hours and fifty minutes. There was no apparent local reaction (N) in 9 of the 15 patients, while 3 patients experienced very little (VL) reaction and 3 patients experienced moderate local reaction (M).

Of the second group of 16 patients, those receiving the 2 percent solution of lidocaine, 5 experienced an excellent response in terms of degree of anesthesia, 9 a good response, and 2 a fair response. There were two complications in this group; the capsules were broken in both cases, however, no observable lens material was noticed in the eyes postoperatively. Seven patients in this second group required no medication and in 2 patients there was no definite data. Of the 7 patients requiring medication postsurgically for pain, the average time after the onset of anesthesia was 4 hours and 24 minutes. No local reaction was apparent in 11 patients in this second group while there was very little reaction in 2 patients, moderate reaction of a local nature in one patient and no available data in two cases.

Conclusions

A unified technique was employed to observe differences between 2 percent and 4 percent lidocaine solutions utilizing a blind technique.

There was no significant difference observed between the two concentrations, either in degree of anesthesia, local reaction postoperatively, or pain in the postoperative period.

Research material for this study was kindly provided by G. Vinton Hallock, M. D., Astra Pharmaceutical Products Inc., Worcester, Mass.

A METHOD OF SUPPLYING PHARMACY SERVICE to outpatient clinics and small hospitals

by GEORGE J. GRUBER

► ONE OF THE MANY CONTROVERSIAL SUBJECTS IN hospital pharmacy today is the provision of pharmaceutical service to small hospitals, clinics and nursing homes too small to economically justify the services of a full-time pharmacist.[1] In many cases these institutions are unable to secure the services of a pharmacist part-time; either because of low salaries or the remoteness of the institution's location. This results in the undesirable situation of the "closet" drug rooms and drug dispensing by nurses or lay personnel. A possible solution to this problem is presented here in an outline of a method of providing pharmaceutical service to several clinics from a centrally located hospital.

There have been various methods proferred by the pharmacy profession to meet this challenging problem. In some instances, a retail pharmacy in the vicinity

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of a small hospital may provide part-time pharmacy service to the hospital.[2] Some small hospitals have solved their pharmacy problems by employing the pharmacist in a combined position—as a pharmacist and as the administrator of the hospital. Occasionally the pharmacist may be employed in a dual capacity as the hospital pharmacist plus additional duties such as that of the hospital laboratory technician or x-ray technician.[1] In other instances, it is possible for two or more of these small institutions, in the same general area, to share the services of a full-time pharmacist.

The U. S. Public Health Service Hospital in Savannah, Georgia, a 150-bed general hospital, has a pharmacy staff consisting of two registered pharmacists and a pharmacy helper. This staffing enables the hospital to take care of its own pharmacy requirements and to provide pharmaceutical service to five Outpatient Clinics of the U. S. Public Health Service. These clinics, located in three states, are as follows: Charleston, S. C.; Atlanta, Georgia; Jacksonville, Tampa, and Miami, Florida.

Basic Principles of Service

During the year 1958 our pharmacy at the USPHS Hospital in Savannah, Georgia, provided a total of 50,041 prepackaged drug units, with a total value of $26,452.16. This pharmacy service has been in operation for over two years and has proven highly successful as an economical means of providing the professional services of registered pharmacists to distantly located outpatient clinics too small to justify the services of a pharmacist of their own. The success of the drug servicing program hinges on the following:

1. Prepackaging of the drugs in quantities commonly prescribed.[3]

2. Swift service—It is essential that drug orders from the various clinics be quickly filled and delivered.

3. Control—Each drug prepackage unit must bear a control number on the label which is duplicated on pharmacy control records. These pharmacy records list the manufacturer's control or lot number, the date of prepackaging, and the initials of the pharmacist responsible for the checking of the prepackaging procedures.

4. Inspection—Periodic visits are made by the pharmacists to the outpatient clinics being serviced by the pharmacy. These visits enable the pharmacist to check the drug stocks for outdated drugs, drug deterioration, proper storage and over-stocking. These visits also provide a valuable exchange of information between the pharmacists and the physicians and nurses at the clinics.

5. Coordination and cooperation between the clinic and the hospital personnel—This is implemented by the equal voice in Pharmacy Committee meetings shared by the physicians at the clinics with the physicians at the hospital. Changes in the hospital formulary or changes in drug unit sizes can be readily instituted by the clinic physicians through the hospital Pharmacy Committee. The physicans are kept constantly informed on drug activities and policies by circulation of copies of pharmacy bulletins, pharmacy committee minutes, and memos.

6. Periodic Review—The pharmacy is constantly on the alert for modifications and refinements to improve the service to the outpatient clinics. The drug requisition forms used by the clinics to order drugs are reviewed and changed annually to include new drugs or delete drugs dropped from the formulary.

Mechanics

The mechanics of the pharmacy servicing of the outpatient clinics are as follows:

1. The outpatient clinic institutes a drug order by filling in the mimeographed drug requisition form (see Figures 1, 2, and 3—the first, second and last pages of our current prepackaged drug requisition form). This procedure involves merely the listing of the number of units desired of a particular drug in the column headed "No. Ordered." The original and two copies of the requisition are made out in this manner and signed by a physician. The original and one copy are mailed to the hospital pharmacy and one copy is retained in the clinic files.

2. Upon receipt of the requisition at the hospital pharmacy, the pharmacy helper fills the order by assembling the requested number of prepackaged drug units. A Senso label, similar to the labels on the prepackaged drug units, bearing the name of the drug and the unit size is affixed to each package of assembled units. The pharmacist checks each item before packaging and initials the requisition.

3. When the order is completed and checked, it is packed in shipping cartons. The pharmacist prices the requisition and totals the cost in the "Total Cost" column. When an item is in short supply or out of stock, a notation is made in the column headed "No. Shipped" and a short note included as to when the item is expected to be back in stock.

4. After pricing, the original drug requisition is placed in pharmacy files and just prior to shipment, the copy is attached to one of the shipping cartons as an invoice. The cartons are then sent by mail or by Railway Express to the outpatient clinic.

5. At the outpatient clinic, the prepackaged drug units are added to the stock on hand and are dispensed by the physician. At the time of dispensing, one of the pair of Senso labels, attached to the prepackaged drug unit, is removed and affixed to a prescription sheet similar to that in Figure 4, or the label is placed directly on the patient's medical record. A

Figure 1.

OUTPATIENT CLINIC PREPACKAGE REQUISITION
U. S. Public Health Service Hospital, Savannah, Ga.

Outpatient Clinic______________________ Req. No.__________

Date Ordered________ Date Req. Received________ Date Shipped__________

Shipped Via__________________ No. Pkgs.____ Packed by____ Inv. Chk.______

ANTIBIOTICS	UNIT	NO. ORDERED	NO. SHIPPED	UNIT COST	TOTAL COST
Bacitracin Ointment 500 U./Gm.	15 Gm.				
Chloramphenicol Capsules 250 mg.	16				
Chlortetracycline Ophthalmic Ointment 1%	5 Gm.				
Chlortetracycline Pharyngets 15 mg.	10				
Chlortetracycline Otic Solution	10 ml.				
Dihydrostreptomycin 5 Gm. vial	vial				
Erythromycin Oral Suspension 200 mg./5 ml	60 ml.				
Erythromycin Tablets 250 mg.	16				
Neomycin 0.3%, Hydrocortisone 0.5% Ophthal. Solution	5 ml.				
Neomycin 0.3%, Hydrocortisone 0.5% Ophthal. Ointment	5 Gm.				
Neomycin 0.5%, Hydrocortisone 2.5% Top. Ointment	15 Gm.				
Neomycin 0.5%, Sod. Propionate 50 mg./ml. Otic Solution F	15 ml.				
Novobiocin, Sodium Capsules 250 mg.	16				
Oxytetracycline Ophthalmic Oint. 1%	5 Gm.				
Penicillin Tablets 200,000 U.	16				
Penicillin G, Procaine, 300,000 U./ml. 10 ml.	vial				
Penicillin G, Potassium 5,000,000 U/vial	vial				
Penicillin G, Benzathine, 300,000 U./ml. 10 ml.	vial				
Penicillin V Suspension 300,000 U./5 ml.	80 ml.				
Tetracycline HCl Tablets 250 mg.	16				
Tetracycline Oral Suspension 125 mg./5 ml	60 ml.				

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ANTIBIOTIC SUBTOTAL ______

COST ______

Figure 2.

ALCOHOL, NARCOTICS, AND HYPNOTICS
(Require Accompanying Prescription with Requisition)

NARCOTICS	UNIT	NO. ORDERED	NO. SHIPPED	UNIT COST	TOTAL COST
A.P.C. with Codeine 32 mg. Tablets	10				
Codeine Sulfate Oral Tablets 32 mg.	10				
Codeine Guai-Ephed Syrup 8 mg./5 ml.	120 ml.				
Camphorated Opium Tincture	60 ml.				
HYPNOTICS					
Amobarbital, Sodium Capsules 200 mg.	10				
Chloral Hydrate Syrup 0.5 Gm./5 ml.	60 ml.				
Paraldehyde	120 ml.				
Pentobarbital, Sodium Capsules 100 mg.	10				
Phenobarbital Elixir	120 ml.				
Phenobarbital Tablets 16 mg.	30				
Phenobarbital Tablets 16 mg.	100				
Phenobarbital Tablets 32 mg.	30				
Phenobarbital Tablets 32 mg.	100				
Secobarbital, Sodium Capsules 100 mg.	10				

Figure 3.

-6-

	UNIT	NO. ORDERED	NO. SHIPPED	UNIT COST	TOTAL COST
Vitamin A Capsules 25,000 U.	30				
Vitamin A & D Ointment, high potency, protective base	60 Gm.				
Vitamin B Complex Tablets	50				
Yeast, Dried, Tablets 0.5 Gm.	100				
Zinc Oxide Ointment	60 Gm.				
Zinc Undecylenate Powder	30 Gm.				
Zinc Undecylenate Ointment	60 Gm.				

TOTAL COST ______

ANTIBIOTIC COST________ TOTAL ITEMS______

REQUISITIONED BY__________________

Figure 4.

M.S.F. PH-1
May 25, 1956

PHS Hospital
Seattle, Washington

Outpatient Clinic Record of Prescription Disposition

NAME: DATE: DOCTOR:	NAME: DATE: DOCTOR:	NAME: DATE: DOCTOR:	NAME: DATE: DOCTOR:
NAME: DATE: DOCTOR:	NAME: DATE: DOCTOR:	NAME: DATE: DOCTOR:	NAME: DATE: DOCTOR:
NAME: DATE: DOCTOR:	NAME: DATE: DOCTOR:	NAME: DATE: DOCTOR:	NAME: DATE: DOCTOR:
NAME: DATE: DOCTOR:	NAME: DATE: DOCTOR:	NAME: DATE: DOCTOR:	NAME: DATE: DOCTOR:
NAME: DATE: DOCTOR:	NAME: DATE: DOCTOR:	NAME: DATE: DOCTOR:	NAME: DATE: DOCTOR:

pressure sensitive label, upon which the directions have been written or typed, is placed over the remaining Senso label on the unit being dispensed (see photo 6). In case a check is required after dispensing the drug, it may be accomplished by peeling the direction label from the container, thus exposing the Senso label beneath (see photos No. 1 and 5).

6. To expedite the filling of drug orders from the outpatient clinics, most of the drugs are prepackaged in the size units listed on the requisition sheet and sufficient stores are maintained so that any one item need not be prepackaged more than once in 30 to 60 days. The prepackaged drug stores thus maintained may also be used in the hospital's own outpatient service.

7. Items called for only occasionally are prepackaged on demand. These occasionally ordered drugs are not listed on the prepackaged drug requisition form but the clinics may derive information concerning their strength and availability from the formulary. The clinics may then order these drugs by typing them in on the blank spaces provided on the last page of the prepackaged drug requisition sheet (see Figure 3).

The outpatient clinic drug orders under the system outlined above are generally filled and shipped within 24 hours of receipt of the drug requisition and a good percentage are shipped within 4 to 6 hours of receipt.

Summary

A system of providing professional pharmaceutical service for five outpatient clinics from one centrally located pharmacy has been outlined. The methods used and the controls effected are thought to be applicable to the problem of providing pharmacy service to small hospitals (under 50 beds) unable to utilize a pharmacist within their own organizational framework. The advantages of this system are:

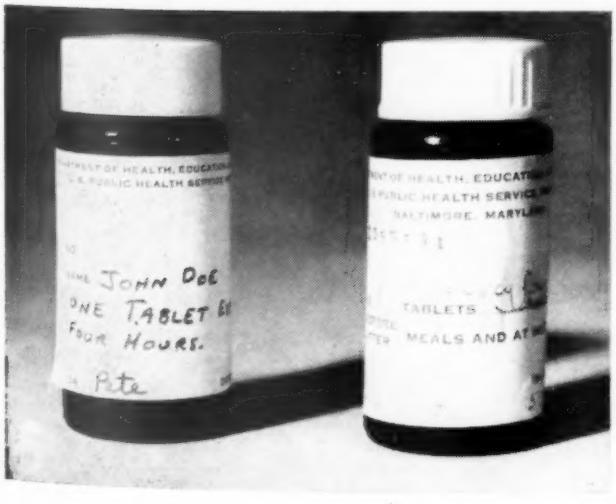
1. The professional services of a registered pharmacist are available.

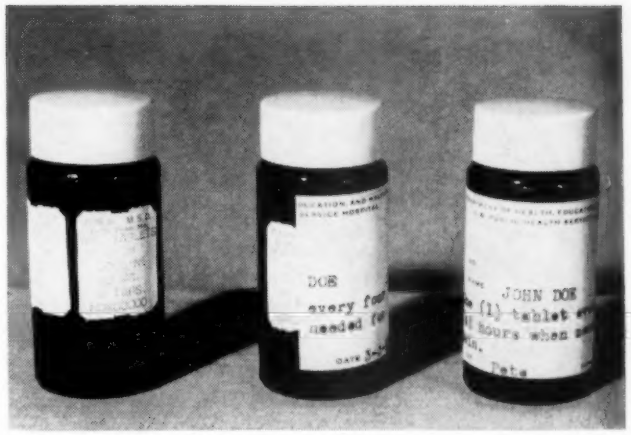
2. Effective controls over the storage and dispensing of drugs are maintained by a pharmacist.

3. Economy of quantity purchasing is obtained by use of a central purchasing source.

4. There is no need for maintaining costly and large inventories at the stations serviced.

Pressure sensitive labels can be placed over the part of the Senso label which remains on the unit being dispensed





A Senso label shown beneath the "Directions" label serves as a control. Note in lower photo that the "Directions" label can be readily peeled off

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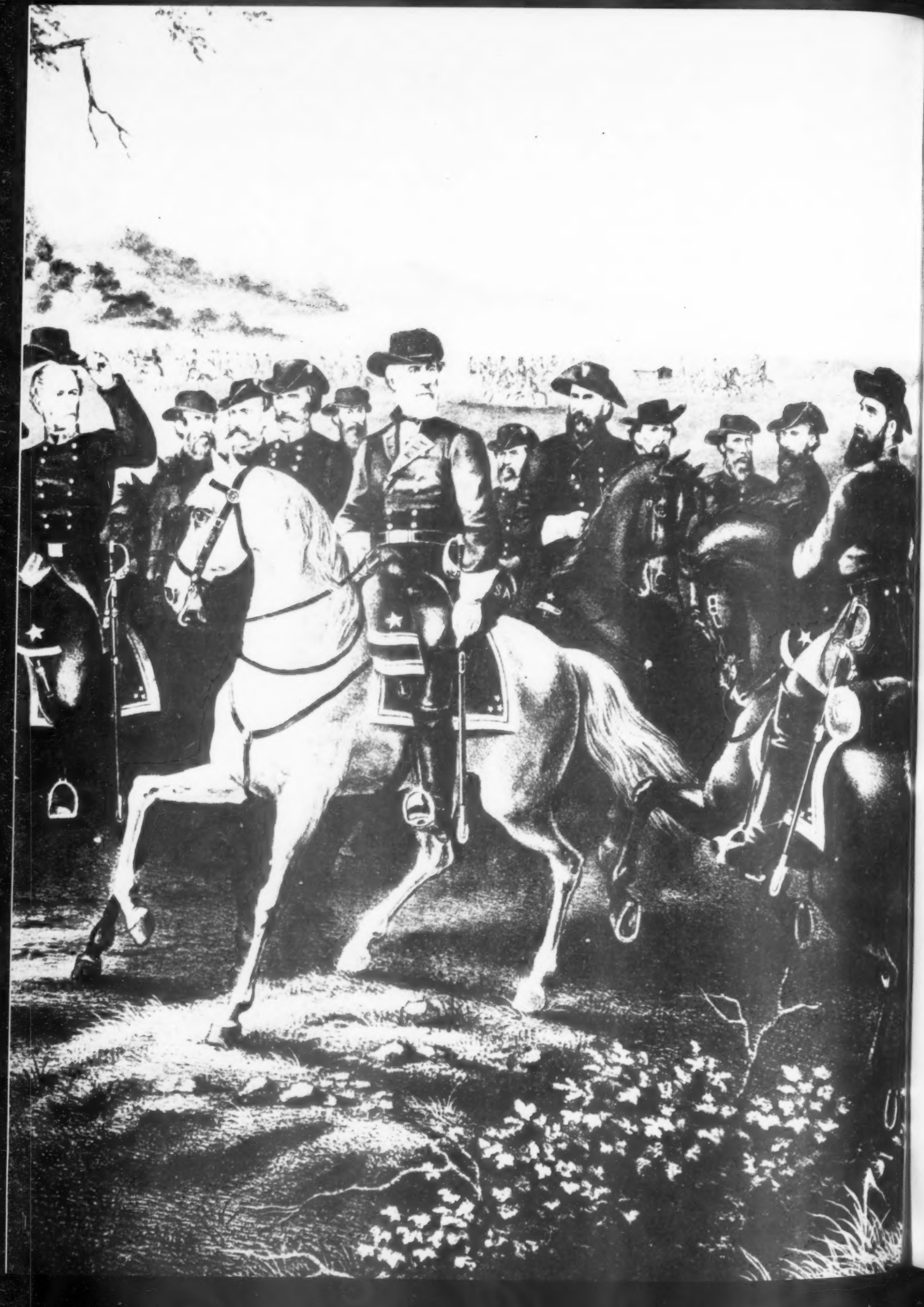
3. Taniguchi, T.: Outpatient Dispensing, *Am. J. Hosp. Pharm. 15*:401 (May) 1958.

4. Wesbury, S.: A Modification of the Prepackaging System for Outpatient Clinics and Offices, U. S. Public Health Service Intern Project Report, USPHS Hospital, Baltimore, Md. Photos 1 and 6 are through the courtesy of Mr. Wesbury.



A CONFEDERATE RECIPE BOOK

by NORMAN H. FRANKE

► IN THE LIBRARY OF CONGRESS A SMALL, TWENTY-four page, paper-bound booklet bears witness to the plight of a heroic but war-ravaged people. Within its pages are more than a hundred recipes designed to bolster the lives of the families of the Southern Confederacy. At least this was the intention when printer G. W. Gray fed the sheets of precious paper into his press for the publishing house of West and Johnson in Richmond in 1863.[1]

Such a booklet was badly needed. For more than two years the Union Armies had been chipping away the body of the Confederate States of America. The Yankee men-of-war closely guarded the Southern harbors. The effect of isolation was being keenly felt by a non-industrial South. As the tattered standards of Dixie were being riddled before Glory's bloody face, the Confederacy impressed many of the necessities of life to supply her armies—necessities that could not readily be replaced. Wages were fixed; prices soared; the dollar inflated; flour and sugar became luxuries. The people of the Southern cities could not generally afford the few items that were available from time to time.

Under such circumstances the appearance of a publication designed to familiarize the townsmen with the various ways of stretching these scarce and costly supplies is understandable.

The "Confederate Receipt Book," as it was called, included formulae gathered from the folk-wisdom of country people versed in the simpler way of living; some, too, were taken from the pages of newspapers. Divided into five sections, the booklet contained recipes for foods, beer, soap and candles, remedies, and miscellaneous items. Like foods and other necessities, drugs were lacking and quite costly when they could be had; therefore, it is not surprising that a pharmaceutical section was included to mitigate suffering from common ills and complaints.

The soap and candle recipes were of some value to the city housewife, especially a recipe for stretching the quantity of soap by adding honey.[2]

The section on food contained substitute recipes for scarce items, such as a pumpkin bread made from pumpkins and unleavened flour, and "mock oysters" made from green corn, eggs, and flour.[3] Such foods, although substitutes for scarce items, contained substances equally lacking in the cities, but readily available to the rural population. Therefore, their actual value to the urban homemaker remains a question; the farming people were already familiar with these recipes. After a study of the recipes it seems that the booklet, although well intended, fell considerably short of its goal.

The section on remedies suggests the same thought. But in retrospect the "old wives" formulae seem scarcely more inadequate therapeutically than does the regular medicine of that period. These recipes do not differ greatly from the folk medicine of the deep South still practiced today.

Let us consider, one by one, the fifteen medical formulae contained in the booklet.[4]

> *For Dysentery, dissolve as much salt in pure vinegar as will ferment and work clear. Use one large spoon of this in a gill of boiled water.*

Vinegar loses its sourness upon standing, and the acetic acid disappears. This fermentation is due to the action of certain bacteria (*Bacillus xylinum* Browne)

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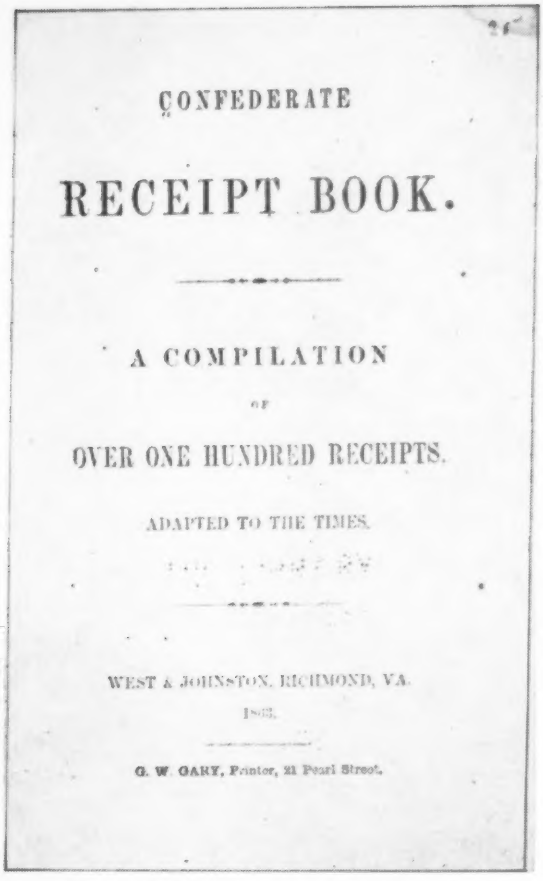
Lee and his Generals, by Charles P. and Augustus Tholey



CONFEDERATE

RECEIPT BOOK.

A COMPILATION

OF

OVER ONE HUNDRED RECEIPTS.

ADAPTED TO THE TIMES.

WEST & JOHNSTON, RICHMOND, VA.

1863.

G. W. GARY, Printer, 21 Pearl Street.

Shown above is the title page from the "Confederate Receipt Book" dated 1863

which, in the presence of air (oxygen) break down the acetic acid into other compounds, including, through the natural oxydases, formic acid.[5] It is doubtful if the salt adds anything to the products of the fermentation reaction. But it is of interest that boiled water was recommended, for polluted water may well have been the cause of the dysentery in the first place, and reinfection was thus prevented. The need for boiled water indicates the ineffectiveness of the remedy as an amebicide or bacillicide. The astringency of the preparation probably provided some slight symptomatic relief.

For Chills, hoarhound. Make a tea and gargle for sore throat.

The dried leaves and flowering tops of this plant (probably *Marrubium canadidissinum, M. peregrinum* (black hoarhound), or *M. vulgare* and species of the genus *Ballota,* especially *B. hirsuta*) contain a bitter principle (morrubin), a volatile oil, tannin, and resins.[6] Now recommended as a bitter tonic and expectorant, the tea would be an astringent and precipitant due to the tannin, as well as slightly antiseptic (a property of all volatile oils). Thus it would be of some benefit in the treatment of a sore throat that so frequently accompanies upper respiratory infections and the chills occasionally associated therewith.

For Diphtheria (sic!) or Scarlet Fever, one cup of milk, two teaspoons of powdered charcoal and ten drops of spirits of turpentine. Soften the charcoal with a few drops of milk, add the rest of the milk and turpentine.

Spirits of turpentine at that time was not a recognized name or synonym for any drug in the *United States Pharmacopeia.* Later (1910) the term was applied to the then recognized oil of turpentine.[7] The rectified oil was not prepared in those days, and the gum spirit was used internally. Thus the distillate of the turpentine oleoresin was the product intended by the term "Spirits of Turpentine." The oil is primarily d-alpha and d-beta pinene with 3 to 7 percent other turpines, alkyl ethers, and esters. A local irritant, the product is but feebly antiseptic.[8] Since it is effective in the relief of bronchitis, and since diphtheria and scarlet fever are accompanied by sore throat and other upper respiratory distress, it is understandable that such a remedy would be tried. (Antitoxins and antibiotics were then unknown, and no worthwhile treatment, save tracheotomy in diphtheria, was available.) The preparation would be ineffective against Lancefield's Group A Hemolytic Streptococci and the *Corynebacterium diphtheriae.* The charcoal could not absorb any appreciable quantity of *C. diphtheriae* exotoxin or of the erythrogenic exotoxin in scarlet fever. It is possible that the value of charcoal rested in neutralizing the carminative action of the gum spirit. But from which ever point of view, we must concede the therapeutic uselessness of the remedy.

For Asthma Relief, use Jamestown weed leaves dried in the shade, saturate with a strong solution of potassium nitrate and smoke it—inhaling.

Datura stramonium L. has long been used in this manner for the treatment of this condition. Commercially available in this form, it is still used today. The weed was common, but the nitrates were impressed for the production of munitions. In fact nitrates were so valued that the celebrated Dr. Joseph LeConte, then director of the Nitre and Mining Bureau at Columbia, South Carolina, requested the ladies of the Confederacy to save their urine so that it might be processed into nitrates.[9] It is doubtful that asthma sufferers could obtain even small quantities of nitrates.

For Croup, apply cold water to the neck.

Relief? Perhaps. Cure? Never!

For Cough, treacle and white vinegar, 24 tablespoons each. 40 drops of laudanum. Give one teaspoon as necessary.

Just what is meant here by "treacle" is a difficult to determine. Perhaps some panacea of the theriac type, perhaps some general folk remedy used for many ills, is intended. It is safe to say that the product had therapeutic merit, if the opium tincture was available. Opium, being an imported product, had to be smuggled in through the blockade, and was also on the list of impressed drugs. It was expensive, and could it be had, only the very wealthy were able to afford it. Without the opium tincture, the merit would rest on the constituents of "treacle." It is somewhat surprising that such a remedy was suggested, for the Southern fields and forests were rich in expectorants.

For Headache, a teaspoon of powdered charcoal and ⅓ teaspoon of soda, mixed in warm water.

This remedy was long used for the relief of cephalagia, and perhaps was the only effective medication in the era of pre-synthetic analgetics. The charcoal would be an absorbent for stomach gases and the soda would overcome the hyperacidity, often the cause of headaches. Whether sodium carbonate (washing soda) or sodium bicarbonate (baking soda) is intended as the "soda" is easy to resolve. Washing soda is a dangerous irritant, especially if used for long periods of time, even in small doses. Then, too, the section dealing with warts (*q.v.*) specifies "washing soda." It is safe to assume that the bicarbonate is intended. And it is of interest here that the term "soda" itself derives from a Latin word meaning "headache."

For Toothache, alum.

Either potassium or ammonium aluminum sulfate is a powerful astringent, irritant (counterirritant), and antiseptic, producing catharsis and emesis when swallowed.[10] This product would have some mitigating action on the pain of dental caries, but pain caused by abscessed teeth would be more difficult to alleviate by this method.

For Burns, wheat flour and water.

Flour and water paste has long been used for its soothing effect on first degree burns, acting as a protective, but grease was plentiful and would have done as well.

For Camp Itch, potassium iodide, 60 grains; lard, 3 ounces, mix. Apply three times a week.

Lard, being an emollient, would both protect and soothe. The potassium iodide would be beneficial also, if available—generally it was not. This remedy was probably included so that, could it be made, it might be sent to a member of the family in the army, where "camp itch" was quite common.

Poultice for Felon—Selma Reporter.[11] *Onions.*

Onion poultices were then, as they are now, popular folk remedies for many conditions, including colds and pneumonia. In the absence of epsom salt such a poultice would be valuable in the treatment of uncomplicated paronychia.

For Corns, lubricate the toe with oil like a "coach wheel."

The oil, any oil—probably corn, cottonseed, or peanut in this instance—would soften the corn and facilitate its removal with a knife.

For Warts, a saturated solution of washing soda.

This caustic,[12] generally effective, would be quite irritating, especially if applied to the healthy tissue surrounding the wart incautiously. If properly applied in a planned course of treatment, the wart would be removed; and it is certainly better than the usual country remedy of burying a dead cat in a graveyard at midnight while reciting an incantation.

For Tooth Powder, powdered charcoal.

A good and serviceable dentrifice, not too abrasive, especially if very finely powdered, it would absorb some of the mouth odors, although thorough rinsing would be necessary to remove the black specks from the teeth.

It will be discerned readily from this consideration of the remedies that three of the recipes are worthless, three are of a questionable nature, one is confusing, one is an unnecessary substitute, and two are decidedly dangerous because inadequate directions for use are given. Of the remedies having some merit, several require ingredients then impossible to obtain or exceedingly costly. In view of these facts one may conclude that the section on remedies, although well meant, probably was not as helpful as some other sections of this interesting "Confederate Receipt Book."

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1. The publishers, West and Johnson, were located at 145 Main Street, and the printer at 21 Pearl Street in Richmond, Va.
2. *Confederate Receipt Book*, Richmond, 1863, p. 11; hereinafter cited as *C.R.B.*
3. *C.R.B.*, pp. 5, 7-8.
4. *C.R.B.*, pp. 13-15, 20.
5. E. O. Jordan, *General Bacteriology*, 1st ed. (Philadelphia and London, 1938), p. 724.
6. Heber W. Youngken, *A Textbook of Pharmacognosy*, 6th ed. (Philadelphia and Toronto, 1948), pp. 736 740-741.
7. H. A. Langenhan, *A Century of the U. S. Pharmacopoeia, 1820-1920* (The University of Wisconsin Pharmaceutical Experiment Station, Madison, Wis., 1923), p. 98.
8. A. Osol and G. E. Farrar, Jr. (editors), *The Dispensatory of the United States of America*, 25th ed. (Philadelphia and Montreal, 1955), pp. 1465-1466; hereinafter cited as the *U.S.D.*
9. A copy of the order may be seen in the Mississippi Room of the Library, University of Mississippi, Oxford.
10. *U.S.D.*, p. 53.
11. A newspaper published at Selma, Alabama.
12. *U.S.D.*, p. 1264.

SUPER

by REED L. CLEGG

► IF YOU DISSECT THE TERM *supervision* you will note it consists of two parts: *Super Vision*. Supervisors are by definition, therefore, superior beings. But are they all endowed with such perfection? "Leader," "boss," "administrator"—these terms conjure various images in our minds as we reflect upon the supervisors we have known, and perhaps have been. I trust these images portray noble and efficient leaders. I am sure, however, the supervisors in our memory have not all been as Caesar's wife, "above reproach." Supervisors are after all just people. They are you and I with our human frailties.

Today I would like to examine with you some of these images, these prototypes of bosses we have known. From these case studies we can deduce general principles of supervision. Most important, we who are or hope to become leaders of men and women can better guide our supervisory behavior. Therefore, let's sketch out some images of supervisors.

The Show Stealer

I am sure none of you has ever encountered the supervisor who insists on hogging the limelight. Yet, this person is a common variety of noxious human being. He proclaims mightily the philosophy of Caesar, "Veni, Vidi, Vinci." For this supervisor it is always "*I* came," "*I* saw," "*I* conquered" with no credit to his people who really did most of the job. To bask in the limelight is a natural instinct. Students of the social sciences tell us that man is motivated by basic urges not the least of which is to seek recognition and acceptance. The true leader, therefore, must subordinate a natural drive to get credit. Better, he should sublimate this drive in terms of receiving his satisfaction through the recognition of his employees. A leader works through others. His accomplishments can only be achieved through the wholehearted efforts of people working under him. Therefore, the best type of leader is the one who plants an idea and then gives others the credit. This type of leader will reap the harvest. A hospital is a fertile setting for the "scene stealer." Hospitals are notorious for harboring prima donnas. Highly trained talented people are oft times of this sort. Therefore, in a hospital environment we have to guard against show stealers.

Laissez Faire and Trouble-Shooting Supervisors

These prototypes of supervisors are opposite in their approach but similar in their results.

The *laissez faire supervisor* is just too lazy to worry about tomorrow. He operates on a false interpretation of Macbeth's musings:

"Come what; come may;
Time and the hour runs through the roughest day."
Like the classical economist, he prefers to let things

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Presented at the Institute on Hospital Pharmacy, Salt Lake City, June, 1959.

VISION

ride. Tomorrow is another day which never arrives for him and, therefore, he is never concerned about future plans.

The *trouble-shooter* is prone to rush around putting out conflagrations after they break out. He is usually lost in details. Some term his disease "detailomania." The trouble-shooter is too occupied in dowsing little fires to plan a prevention program.

Both of these types of supervisors have one obvious deficiency in common. They fail to look ahead. They neglect miserably to plan their functions or to schedule the work of their people. Too many of us consider planning as a side activity which has the tinge of illegitimacy. People somehow are a little ashamed of sitting back and trying to forecast future events even though such efforts are vital to their role as a supervisor. A leader must plan ahead. As Fayol said, the true leader must exercise "prévoyance." Fayol indicated that the leader or supervisor must not only forecast the future but he must make specific plans to meet that forecast.

The Vocalist

Sometimes I wonder if "anybody is listening." It is a human attribute to want to do all the talking and none of the listening, and supervisors are human. They say that some people acquire a large vocabulary the hard way—by marrying it. However, I am inclined to feel that our urge to dominate the conversation is more instinctive than that. Again, a good supervisor must sublimate his urge to dominate the conversation. He must be a good listener. Good listening implies more than keeping silent. You must be an attentive listener, trying to hear and understand what the other person is expressing. Shuffling papers and looking afield only distracts the person and he gets the impression you are not interested in his problems. It is an interesting fact that if you let a person talk through his problems he will usually arrive at the solution on his own. How many times have you talked it out with somebody and found that by so doing the solution became obvious to you? A whole technique of psychology is predicated on this simple plan of letting the person talk out his problems. Try being a good listener. You will not only learn a great deal but your subordinates will also.

The Self-Made Man

This supervisor follows the injunction, "Each man for himself—the Devil take the hind most." He came up the hard way and expects everybody else to do the same. You all recognize this prototype of the aggressive person who strove from rags to riches with an indomitable will to succeed. For his tenacity and energy we can only give full credit. He has many virtues but he has the damaging fault of not helping his subordinates to succeed. Some experts claim that half of a supervisor's job is to prepare his people for greater accomplishment. The self-made man sees no necessity for aiding his subordinates in this manner. His attitude tends to discourage self-development of his people.

We must remember that no man is an island. If he is to succeed as a leader he must encourage his people to grow and to expand their spheres of endeavor. He

must seek tangible means of training his people for greater things.

Unpredictable Supervisor and Sacred Cow Supervisor

Strange bed fellows these two villians but in a sense they are cast from the same mold. At least, the havoc they wreak is equally disastrous.

The *unpredictable one* follows, out of context, Emerson's thought, "Consistency is the hobglobin of little minds." This supervisor is unpredictable in his own personal behavior. One day he may greet a subordinate profusely and take half an hour to share that man's personal experiences. The very next day he may cut off the same man with a curt nod of the head or with an obvious "don't bother me" manner. The devastating effect one's changes in behavior can have on other people is amazing. You have all been hurt by a friend who unconsciously turned you aside or treated you differently than he ordinarily does. It doesn't have to be a change from the better. A person can be jolted just as severely by the boss who normally is curt and impersonal but suddenly becomes the good fellow type. This abrupt change in behavior pattern arouses suspicion and uncertainty among the group. It does so because the group members cannot predict the boss' behavior or his motives. There has to be continuity in the work situation, too. When changes occur, and of course there must be progress, these changes must be carefully introduced. They should not be the fly-by-night variety.

People react favorably when they have fixed standards to meet. If employees have a measuring rod against which they can compare their performance they produce more efficiently. They prefer a work standard to a nebulous land of no specific goals or requirements. It is a fundamental need of all of us to be able to predict the behavior of others. Certainly a supervisor must fulfill that need.

The *sacred cow supervisor* is just the opposite. "Don't destroy our heritage" is his watchword. He holds to tradition and to the old ways of doing things. This poor leader is a stifler of initiative and a killer of creativity. He is afraid of making mistakes and, therefore, makes no progress. To paraphrase Mark Anthony, "The good is oft interred with our boners." This fault of a supervisor is obviously one to shun.

There is a happy medium between doing nothing and doing everything at once unannounced.

Bull in a China Shop Supervisor

How many supervisors have you known who possess good ideas and splendid principles but they introduce them at precisely the wrong moment? There is a time and a place for everything. Timing is as important as knowing what to do. This is a pitfall plaguing most supervisors. There is no magical formula by which we can gauge the propitious moment. Knowing when to introduce new ideas is almost instinctive. Yet, by experience and by a conscious awareness of the importance of proper timing, we can improve in this vital area.

The Indecisive Soul

Have you known a boss who could not make up his mind? I've almost come to believe that this failing is congenital. There are those individuals who seemingly cannot arrive at a decision even of the most simple variety. These individuals make the world's worst leaders. For again, people need certainty; they need predictability; they need to know what is coming next. The indecisive soul has a concomitant failing. After he has finally ventured an opinion he seeks to shift the blame onto everybody else. This person will invariably call you in to serve as a consultant when the antagonists lay down the gauntlet. You all know the classical definition of a consultant. He is the man who is called in at the last minute to share the blame.

Making decisions is really not so difficult. Nor need it be an arbitrary process. Mary Parker Follett argues that if a supervisor will assiduously collect all the facts about a situation and will carefully analyze all of these facts, the decision is almost an automatic result. Too often we supervisors make snap judgments based on no investigation or analysis. An ill considered decision is damaging but not nearly as devastating as no decision at all. There is the happy medium, however. Collect and analyze all of the facts available and then make up your mind within the appropriate time limits.

At some time in our hospital experience we have encountered prototypes of these supervisors. Perhaps not in the pure form as caricatured above but the faults portrayed are widespread among us supervisors. I hope this points up the obvious moral that each supervisor should "know thyself." Socrates said this a long time ago. He must have had leaders of men and women specifically in mind. A real leader must strive to understand his own motives and behavior. He must seek to sublimate the natural expression of his own drives to the betterment of the group. In so doing he himself will be a better leader and will profit thereby.

A Chinese philosopher, Lao-Tzu, expressed my thesis very well:

> A leader is best
> When people barely know that he exists,
> Not so good when people obey and acclaim him,
> Worst when they despise him.
> "Fail to honor people,
> They fail to honor you";
> But of a good leader who talks little,
> When his work is done, his aim fulfilled,
> They will all say, "We did this ourselves."

ABSTRACTS OF PAPERS

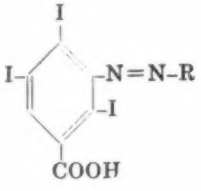
presented at the 19th International Congress of Pharmaceutical Sciences of the International Pharmaceutical Federation Zurich, Switzerland, September, 1959

A series of abstracts presented at the 19th International Congress of Pharmaceutical Sciences of the International Pharmaceutical Federation is appearing in THE JOURNAL. The first of the series appeared in January. In this second series, abstracts presented in English are continued and the beginning of those translated from German.

RADIOPAQUE COMPOUNDS

Synthesis of 2,4,6-Triiodo-3-(aminopyridylazo) Benzoic Acids and Studies on Their Roentgendiagnostic Properties, by H. Bojarska-Dahlig and P. Nantka-Namirski (Department of Synthesis, Institute of Pharmacy, Warsaw, Poland.)

In continuation of studies on radiopaque compounds and in connection with the published data concerning an accumulation of neotropine—a clinically efficacious urinary tract disinfectant—in the gall bladder and pancreas, we have prepared for pharmacological evaluation a number of azo derivatives of 2,4,6-triiodo-3-aminobenzoic acid. These compounds are of the general formula:



wherein R is pyridyl with OH and NH_2 substituents. They were prepared by interaction of diazotised 2,4,6-triiodo-3-aminobenzoic acid with various pyridine derivatives. The products of reaction with 2,6-diamino- (I), 2-hydroxy-6-amino- (II), 2,6-diamino-4-hydroxy- (III) and 3,5-diaminopyridine (IV) were tested in mice for acute toxicity and in dogs for roentgendiagnostic properties. 2,4,6-Triiodo-3-aminobenzoic acid (V), its pyridine salt (VI) and 3,5-diiodo-2,6-diaminopyridine (VII) were also tested and results compared with those obtained for azo derivatives. Substances I, III and VII are practically not toxic in oral administration. Substances I, II, III and IV when administered intravenously as high concentrated solutions of N-methylglucamine salts had LD_{50} little lower than 1 g/kg. Substances I, V and VII gave faint gall bladder shadows after oral administration. When compounds I, II and III were given intravenously as their N-methylglucamine salts solutions the cholecystogram has shown much better visualisation. Compounds II, III, IV and VI after oral, IV also after intravenous administration gave no gall bladder contrast. The elimination of substances under test was principally via the colon, partly also via the urinary tract. On histological examinations no acute inflammatory changes after administration of tested azo derivatives have been found. The investigation is being continued.

A THIRD DIMENSIONAL APPROACH

Stereochemical Factors in Medicinal Chemistry, by Arnold H. Beckett (Chelsea School of Pharmacy, Chelsea College of Science and Technology, London, England.)

The majority of chemical substances formed and broken down in metabolic processes are optically active. The penetration of certain membranes is stereospecific and the uptake of enantiomorphs upon naturally occurring surfaces is selective. A three dimensional approach to drug design therefore seems essential. Such an approach is illustrated by investigations of drugs acting at the central nervous system.

Analgesically active enantiomorphs are shown to have the same spatial arrangements. The use of stereoselective adsorbents in such investigations is described. A consideration of these spatial arrangements leads to the delineation of the analgesic receptor surface. Physico-organic studies indicate that molecules such as those of the methadone, thiambutene, pethidine and prodine-types exist in conformations which facilitate fit at the analgesic receptor. The use of conformational considerations of the stereochemistry of addition to ketones, of the rates of hydrolysis and elimination of esters, and of the infra-red spectra of certain alcohols and esters are used to elucidate the configuration of prodine-type analgesics. A consideration of the implication of oxidative dealkylation at the receptor site is given and the design of suitable analgesic molecules discussed.

The importance of steric factors in certain biological processes is presented. The planarity of important surfaces of drugs may be altered by making use of the introduction of small steric factors with consequent effect upon restricted rotation of suitable ring structures. Ultra-violet evidence is presented as a semiquantitative measure of these effects.

ASSAY OF CONIUM MACULATUM

The Determination of the Alkaloids of Conium maculatum L. by Paper Chromatography and Other Methods, by J. W. Fairbairn and P. N. Surwal (School of Pharmacy, University of London, England.)

The major alkaloids of *Conium maculatum* L. are coniine, methyl coniine, γ-coniceine and conhydrine. Early methods of assay merely determined the total alkaloids, either gravimetrically or titrimetrically, and required comparatively large quantities of material. Since we wished to trace the changes in the alkaloidal picture during the development of the flower into the fruit we needed a method of assay which would require only small samples of material and would determine the individual alkaloids. For this purpose we tried paper chromatographic methods, using *tert*-pentanol/*tert*-butanol/*N* HCl (9:2:2) as running solvent, by ascending technique. The spots were revealed using bismuth iodide reagent (*Munier* and *Macheboeuf*); coniine had an R_f value of 0.66; methyl coniine of 0.55; conhydrine, 0.43 and γ-coniceine 0.32. Attempts were then made to assess the quantities of alkaloids in plant extracts by measurement of the spot areas, using pure alkaloids as standards and about 10 replicate chromatograms for each determination. It was interesting to note that for a given weight of alkaloid γ-coniceine gave an area about five times that of coniine. This fact will be commented on. Band chromatograms were also run and the larger amount of alkaloids obtained were eluted from the paper and determined spectrophotometrically (*Fairbairn* and *Challen*). A third method of determination was also used, namely the simultaneous measurement of spot area and colour intensity by means of a suitable densitometer. The results of all three assays are compared and discussed.

The following abstracts of papers presented at the 19th International Congress of Pharmaceutical Sciences were translated from the German by Mr. Otmar M. Netzer of the School of Pharmacy, San Francisco Medical Center, University of California, San Francisco.

GLYCO-ALKALOIDS FROM S. DULCAMARA

A New Method of Separating Glyco-alkaloids from Solanum dulcamara L. (Eine neue Methode zur Trennung der Glycoalkaloide von Solanum dulcamara L.), by H. Sander, M. Alkemeyer, and R. Hänsel. (Institut für Pharmakognosie, Freie Universität, West Berlin.)

Experiments with tomatin showed that this tetra-saccharid as well as the demissin combines with cholesterin to form molecular compounds insoluble in 96% ethanol. The solubility of these cholesterides was compared with the analogical digitonin-cholesterid and a new method to split them was suggested.

Applying this to the glycoside mixture of the leaves of *Solanum dulcamara* it results that it may be fractionized with cholesterin. The soladulcidin-tetraoside precipitated by cholesterin was prepared pure, Fp. 268-70° C. (decomposition), [alpha]D = -53°. It contained two moles glucose, one mole galactose and one mole xylose as well as the aglycon soladulcidin (5 alpha-solasodanol). In the filtrates of the cholesterin precipitate di- and monosaccharides were found which did not contain xylose but rhamnose. The percentage of soladulcidin-tetraosides in the total glycoside mixture varies with the various parts of the plant. There are origins of *Solanum dulcamara* in which soladulcidin exists only in traces; instead a new aglycon, soladulcamaridin, was found, the constitution of which is not yet certain.

The very slow solubility of the steroidalkaloid-tetraosides as cholesterin-molecular compounds may also be employed in their quantitative assay.

CHROMATOGRAPHIC DIGITOXIN

Column-chromatographical Procedure to Determine Digitoxin in Digitalis Leaves (Über ein säulenchromatographisches Verfahren zur Digitoxinbestimmung in Folia Digitalis), by F. Neuwald. (Staatsinstitut für Angewandte Botanik, Universität, Hamburg, Deutschland.)

A quantitative assay method which would permit a faultless judgment of the official *Digitalis purpurea* for use in pharmacy for prescriptions as well as for manufacturing has so far been an unsolved problem of digitalis research. The determinations by the official bio-assay methods were not satisfactory as numerous publications show. The reason is the digitalis leaves are used in the pharmacy mainly for oral therapeutic preparations and are dispensed as such. The bio-assay is carried out in animals by parenteral injection with drug extractions and only a toxic value is determined.

Since biochemical digitalis research has shown successful ways of gaining glycosides in preparations, effective in heart therapy, there resulted the possibility of analysis to determine the therapeutic main glycoside digitoxin alone and thereby the possibility of working out a method not unsimilar to the determination of morphine in opium. The authors succeeded in isolating the chloroform-soluble glycosides quantitatively from an aqueous solution after reducing the genuine primary glycosides by fermentation into secondary glycosides and purification, and they succeeded in dividing the glycosides by the use of different solutions on a column of alkali-free aluminium oxide into fractions. On this occasion, in one fraction, the entire digitoxin was found together with strospeside and gitoxigenin, and in this fraction the digitoxin alone may be determined photometrically with xanthanol according to the method of *Pesez*. The assay of numerous domestic and foreign digitalis leaves in this manner showed an average content of digitoxin of 0.12% with maximal differences up to ± 20%. This method was easily reproduced.

RADIOISOTOPES IN ASSAY

A Few Possibilities to Apply Radioisotopes in Drug-Assay (Einige Möglichkeiten der Ausnützung der Radioisotope in der Arzneimittelkontrolle), by J. Majer, M. ŠarŠúnová and J. Tölgyessy. (Kreiskontrollaboratorium der Kreisapothekerleitung, Pharmazeutische Fakultät, Bratislava, Tschechoslowakei.)

Within the framework of studies on the possibility of using radioisotopes for the control of drugs the authors worked out a radiometric determination of drugs containing potassium by determining the ^{40}K existing in constant quantity in all salts and which is independent of their age or origin. Furthermore a method was worked out with a precipitation reagent, the active 0.1 N $^{204}TlSO_4$, to determine radiometrically the iodine and the iodides of Solution Jodi spirituosa and of Lugol's solution.

In a further series of experiments they also determined radiometrically zinc oxide, calcium salts, elementary sulfur, and organically bound sulfur in official ointments, pastes, liniments or in other drugs often used in compounding prescriptions. The radiometric method proved itself to be exact and quick in all analyses carried out.

RADIOCHROMATOGRAPHIC METHODS

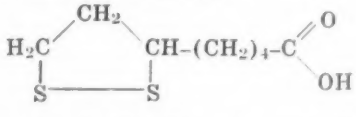
The Radiochromatographical Determination of Alkaloids in Nux vomica Tincture and Extract (Die radiochromatographische Bestimmung der Alkaloide in Tinctura und Extractum Strychni), by M. SarSúnová, J. Tötgyessy and J. Majer. (Kreiskontrollaboratorium der Kreisapothekerleitung, Pharmazeutische Fakultät, Bratislava, Tschechoslowakei.)

A chromatographic method was worked out to distribute strychnine and brucine in nux vomica tincture and extract with a following radiometric evaluation of the isolated alkaloids. The distribution was effected in neutral water-saturated butanol with the method of descending chromatography in chambers 10 x 25 x 47 cm. at T = 18°C. ± 2°C. The work was done on Whatman No. 1 paper. The chromatographic isolation of the two alkaloids took 16 hours. The isolated alkaloids as well as the standard substances, which were chromatographed at the same time, were developed by dipping them into an active solution of phosphomolybdic acid which was marked with ^{32}P. The developed chromatograms were then washed five times within ten minutes with a mixture of 9 parts of distilled water and 1 part of hydrochloric acid 25%. In this way the excess of active phosphomolybdic acid was washed out, and only the precipitate of the phosphomolybdic acid with the alkaloids isolated from the galenical preparations remained active. The activity of the precipitate, isolated from the galenical preparations, and of the alkaloids chromatographed at the same time, which were treated in a similar manner, were compared according to their radiometric and radioautographic evaluation. From the measured activities of the standard alkaloids, on one hand, and of the alkaloids isolated from the galenical preparations, on the other, the alkaloid content of the preparations analyzed was calculated.

THIOCTIC ACID IN LIVER DAMAGE

Curative and Preventive Protection of the Liver by the Use of Thioctic Acid by Application of Phenothiazine (Präventiver und kurativer Leberschutz durch Thioctsäure bei Phenothiazinapplikation), by W. Ritschel. (Pharmazeutisches Laboratorium GIROL AG, Zürich.)

At first the preventive and curative protective effects of thioctic acid, 6,8 -dithiocaprylic acid,



were tested in allylalcohol tests with guinea pigs and rabbits in order to determine whether or not these animals could be considered useful for tests of this kind. Since this was proven, in both kinds of animals the following test series were conducted: (1) control animals not treated; (2) application of phenothiazine in different dosages; (3) application of phenothiazine in different dosages; after discontinuing the phenothiazine a following application of thioctic acid in different dosages; (4) simultaneous application of phenothiazine and thioctic acid, and various relations of the two drugs, in different dosages; and (5) application of the lethal dose of phenothiazine alone, and with simultaneous application of thioctic acid.

Thioctic acid was administered in parenteral solution I.M. Phenothiazine was given I.M. as 10-(3-dimethylaminopropyl)-phenothiazine hydrochloride.

The livers of the test animals were preserved partly in 4% formalin and partly in 70% alcohol. After the usual coloring they were histologically examined. (The results of the histological evaluations will be discussed at the convention.)

In summary, in animals with liver toxicosis caused by 10-(3-dimethylaminopropyl)-phenothiazine hydrochloride the necrotropic liver protecting effects of the 6,8-dithiocaprylic acid were tested. It showed that 6,8-dithiocaprylic acid is effective in the prevention as well as in the cure, while stating that the simultaneous application of phenothiazine and thioctic acid a dosage in the ration of 1:1 is already an effective protection of the liver.

If thioctic acid is used only after the discontinuance of phenothiazine in already existing liver damage, it must be applied in a relation 2:1 to the phenothiazine in order to obtain curative results. The mechanism of action is not yet clear. It is probably based upon the quality of the saturated heterocyclic five-ring system which is being transferred as proton-acceptor into the corresponding aliphatic disulfydryl-combination and may interfere with red-ox processes.

VINCA MINOR

New Knowledge of Vinca Minor L. (Neue Erkenntnisse über Vinca minor L.), Z. Cekan, J. Trojánek. (O. Strouf and K. Kavková, Forschungsinstitut für Heilpflanzen, Prag, Tschechoslowakei.)

The authors are engaged in a study of the chemistry and pharmacology of the *Vinca minor*, the lesser periwinkle, in particular, because the plant is so closely related to the species Rauwolfia. In chemical as well as in pharmacological respects new knowledge was gained of this plant. Concerning the chemistry of the *Vinca minor*, they succeeded in separating vincamine from isovincamine through a new procedure.

From the mother liquor, after the vincamine fraction, were isolated two isomeric indol-alkaloids which have not been previously described, the vincaminorin and the vincaminorein, by a combination of the *p*H-conditions with the distribution chromatography. These substances are characterized by infra-red and ultra-violet spectra; for them was determined the empirical formula, and the character of the functional groups and systems were found for the separation by paper chromatography.

The pharmacological department observed that in acute tests with cats and rats, with a normal blood pressure, and rats with experimental hypertension, vincamine in dosage of 50-100 γ/kg effected a prolonged and probably centrally conditioned lowering of the blood pressure. After a higher dosage this depression does not take place. This knowledge combined with the study of the mechanism of action brings a new idea on the pharmacodynamic effect of vincamine.

ERYTHROXYLUM COCA

Studies of Erythroxylum Coca Lam. (Untersuchungen mit Erythroxylum coca Lam.), R. Hegnauer and L. H. Fikenscher. (Pharmazeutisches Laboratorium, Universität, Leiden, Holland.)

On the basis of studies of the literature and their own tests, the authors are of the opinion that the commercially available coca leaves (Bolivia-leaf, Truxillo-leaf, Java-leaf) are derived from different varieties of one single cultigene species, *Erythroxylum coca* Lam. Within this species three main varieties may be distinguished:

var. *coca*: furnishes the Bolivia-leaf type
var. *truxillense* Rusby, pro spec: furnishes the Truxillo-leaf type
var. *novogranatense* Morris is cultivated in Columbia: the leaves are not commercially available.

The coca variety is being understood as a mountainous type of the species which thrives mainly in the tropical flat-country.

Studies about the ontogenesis and the distribution of the alkaloids lead to the following main conclusions:

1. The ecgoninebases are produced within the leaf. Primarily methylecgonine is probably produced.
2. Kuskohygrine is also produced in the leaf.
3. Hygrine, pseudotropine and tropacocaine are probably formed by the roots.
4. The plant also contains nicotine and others not yet known, tropine or pseudo tropine derivatives. These bases are probably formed in the root.
5. The alkaloid content of root, trunk, and branches is very low. Only the leaves contain much alkaloid. Since, in that case, the ecgoninebases are in the majority *Erythroxylum coca* must be considered as a species which forms its alkaloids mainly in the leaves.

DIASTEREOMERE GLYCOSIDES

Diastereomere Naringenin Glycosides in Salix purpurea (Diastereomere Naringeninglukoside in Salix purpurea), R. Hänsel, D. Heise und G. Pinkewitz. (Institut für Pharmakognosie, Freie Universität Berlin.)

C. Charaux and *J. Rabaté* (1931-1933) isolated salipuposide (melting point 227° C.) from *Salix purpurea* and recognized it as naringenin-5-beta-D-glycoside, which furnished, when hydrolized in formic acid-glycol, the optical inactive ($\pm$) -naringenin as the aglycon. Different from this is the naringenin-5-beta-D-monoglycoside (melting point 160° C. corr.), which was first isolated from *Helichrysium arenarium*, then from *Salix purpurea*, by means of carefully chosen methods; it gives under the same conditions the optical active (-) -naringenin $[\alpha]_D^{20} = -35.2°$ (pyridine). These observations led to the assumption that the salipurposide synthesized for the first time by *A. Zemplen* and co-workers (1943) was not a uniform composition. The compound was therefore again synthetically produced; it showed all the characteristics given for salipurposide, but separated on paper chromatographically, in the medium glacial acetic acid : water (15 : 85), into two substances with the R_F values of 0.51 and 0.63; as substances for comparison were employed at the same time: naringenin (0.22), isosalipurposide (2', 4, 4', 6'- tetrahydroxychalcon-6'-D-glycoside; 0.16), naturally occurring salipurposide (0.51 and 0.63), (-) -naringenin-5-beta-D-glycoside (0.51). It is possible, when treated with sodium acetate, to transform the latter compound (melting point 160° C., $R_F = 0.51$) over the chalcon form into the salipurposide (melting point 227° C.; $R_F = 0.51$ and 0.63). It has been concluded that the salipurposide, which is difficult if possible at all to split by crystallization, is a "mixture" (molecular compound?) of two diastereomere naringenin-5-beta-glycosides, differing from each other by the configuration of the aglycon component.

PURITY TESTS

A Few Problems of Pharmacopeia Purity Tests (Einige Probleme der Pharmakopöe-Reinheitsprüfungen), by L. Mittelmann. (Eidg. Pharmakopöekommission, Bern, Schweiz.)

In tests for purity the immense variety of combinations of quantity, binding, character, and carrier substances presents to the drug analyst a tremendous number of problems which he can solve only by using a corresponding number of test and determination methods. The problems which must be solved are various and of different nature.

A few of them are: (1) the definition of pharmaceutical purity; (2) the method of determination of purity; (3) the value and the usefulness of several physical pharmacopeia test methods (melting range, optical rotation, UV-light absorption etc.); (4) the difference between the proof of inorganic and organic contaminations; (5) the importance of sensitivity, reproduction, and specificity of the chemical test methods; and (6) the part of the *p*H, the carrier substance and the test conditions.

These problems are generally discussed on hand of a few practical examples (ammonia, potassium, phosphate, nitrate, etc.).

It is practically impossible to work out general methods for the pharmacopeia which are useful for a "border test," and which, if possible, always under the same test conditions, may be used with a greater number of pharmacopeia substances. Besides, the method should be specific, but in any case selective, sufficiently sensitive, easily and quickly applicable, and furnish all values which may be reproduced. General methods which correspond completely to all these demands are not numerous. Accordingly, the analyst must in many cases be satisfied in using methods which constitute a certain compromise.

TO BE CONTINUED

no 1

a commentary on the KEFAUVER HEARINGS

by Robert P. Fischelis

► "MANY AMERICANS MAY BE PUZZLED by or indifferent to the space race and confused by talk of missile and/or deterrent lags. But they know what hits them when they pay 50c to a $1 per pill for medicine prescribed by the doctor." So writes Marquis Childs, the well-known newspaper columnist, in one of his recent contributions to the *Washington Post*. We do not have to agree with the figures cited by Mr. Childs or the so-called profit margins quoted by the staff of the Kefauver Committee in the investigation of the drug industry now in progress in order to appreciate the implications in Mr. Childs' statement.

The information which is being developed as the principal executives of some twenty drug manufacturers are being questioned before the Kefauver Committee on the policies of their firms with relation to the acquisition of patents, patent licensing procedures, price structures, profits, and policies with respect to advertising, merchandising and distribution, has made newspaper headlines all over the United States. To what extent this may have shaken public confidence in the procedure by which the fruits of pharmaceutical

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and medical research are brought to the sick, remains to be seen.

Obviously, the distribution of drugs through hospitals and the participation of hospitals in clinical research, so necessary to develop the potential of newly discovered drugs, are matters of interest to hospital pharmacists. This particular segment of our profession is also vitally concerned with the impressions that go out to the public about medical care in general.

As a matter of fact, hospitals have not escaped criticism in these hearings. It has been alleged, for example, that the high cost of drugs, as recorded in the bills of those who have been hospitalized, may be due, in part at least, to the effort of some hospital administrators to recover losses in other departments of hospital service by charging as "much as the traffic will bear" for drugs which are administered to hospital patients.

An unfortunate factor in public hearings before Congressional bodies is that very frequently the detailed answers to questions, which are necessary to bring all of the facts before the investigators, do not catch up with the newspaper headlines which are based on whatever has been said up to the time the papers go to press.

Eventually, of course the whole story is unfolded, stenographic reports are reviewed, records are corrected, false allegations are refuted, and the record is printed in the form of reports from the committee. Also the final recommendations, which may or may not lead to proposed legislation, are recorded in these reports.

The Approach

The Kefauver Committee staff has proceeded on the basis that information with respect to "administered prices" in the drug industry could best be developed by selecting categories of drugs and dealing with any patents involved; costs of production; selling prices to hospitals, government agencies, foreign agencies, wholesale and retail pharmacists; and the policies of the manufacturers concerned with respect to patent licensing, alleged monopolistic procedures, and profit margins.

So far, information has been developed along these lines with respect to cortisone derivatives and the so-called tranquilizer drugs. Representatives of the principal manufacturers of these drugs have been heard. In the early stages of these hearings, the spokesmen for industry were at some disadvantage because they were not familiar with the direction the inquiry would take, but as the line of questioning continued, a definite pattern was established as outlined in the preceding paragraph.

Answers to the committee's questions have, in general, been remarkably frank and, while newspaper reports have tended to emphasize "high prices," "huge profits," "monopolistic tendencies," and played down the effective replies of industry spokesmen to these assertions, there was a better and fairer presentation of both sides of the case as the hearings progressed and industry spokesmen came better prepared to answer the committee's leading questions.

The final public reaction with respect to what is published in the newspapers about these hearings will depend on the general intelligence and ability of readers to analyze the information presented. But as far as the average citizen is concerned, he will undoubtedly interpret what he reads in the light of his personal experience.

Emotionalism Involved

Pharmacists can talk themselves blue in the face about the reasons why a certain prescription costs what it does. But, if the financial impact on the user of that prescription has been catastrophic, his emotional response will correspond to the degree of the impact.

There is no question that a kind of resentment has been built up in recent years with respect to alleged increasing costs of prescription medicine. That is why the matter has reached a point where a Congressional investigation did not seem out of line to the members of Congress and why it has not been difficult for Senator Kefauver to obtain a substantial appropriation, approaching a half million dollars, to carry on his inquiry.

The fact that this committee is known as the Subcommittee on Antitrust and Monopoly and is a part of the Senate Judiciary Committee and that the specific authorization under which this inquiry is being conducted is to investigate "administered prices in the drug industry to determine whether consumers and the public interest generally are being adequately protected by the force of competition" is of no great importance to the man in the street. All he thinks about is that "prescription medicine," according to his idea, costs *him* too much and that he is glad Congress is apparently going to do something about it and he is in favor of that.

Points At Issue

Even though the hearings have thus far covered only an investigation of "administered prices" with respect to cortisone derivatives and tranquilizers, it is quite probable that most of the points to be brought out in the investigations have already been touched upon. They include: public policy with respect to issuing patents on drugs and the 17 year monopoly involved; process patents versus product patents; the use of trademark laws for the perpetuation of exclusive rights

in the marketing of drugs on which patents have expired; the cost of research involved in the birth of a new drug and its proper production in safe dosage form with all that this involves in bringing it from the test tube stage to the bedside of the patient; the system of distribution from the manufacturer to the wholesaler, retailer, hospital, physician and patient; advertising, promotion and detailing.

This commentary is being written just prior to the next stage of the Congressional inquiry which will bring to the hearing on February 23 President Austin Smith of the Pharmaceutical Manufacturers Association for a general statement and questioning which will provide an opportunity to tell what is involved in bringing the fruits of modern science to the sick.

Mrs. Mildred Brady of the Consumers' Union is scheduled to appear on February 24, and two physicians, who were formerly associated with drug manufacturing firms, are scheduled to testify on February 25.

It was announced when the hearings were started that Senator Kefauver expected to confine them to the investigation of "administered prices" in the drug industry and that he would not get into the wholesale or retail distribution of the products of the industry. That such a limitation is not within the realm of possibility is already apparent from the information that has been developed in the hearings to date.

Apparently, the general public reaction to the headlines which have appeared in the press, and to the editorial comment and review of the information developed at the hearings, in such publications as *Time, Life, Newsweek,* and others, echoes Mr. Kefauver's oft repeated statement that "drug prices are too high." This seems also to be the general attitude of the more sophisticated professional and business people in other fields who know what elements go into the makeup of the prices of commodities and professional services.

Function of Pharmacist Challenged

What is of deeper significance to the profession than the immediate reaction to the problem of lowering the costs of drugs is the possible effect of an adverse public reaction on the future of the practicing pharmacist. The public is becoming aware of the fact that in the retail pharmacy he does not any longer function to a great extent as a compounder of prescribed medicines. The incisive question has been asked, "what does the pharmacist do for what we, the public, pay him, when we ask him to dispense a physician's prescription?"

The public must be made more aware of the importance of the services that bring essential drugs from their many sources to the wholesale and retail supply stations and to hospitals throughout the United States. The mere existence of a drug is of little help to the sick. Accessibility to the drug if, as and when needed, in proper dosage form for immediate use, is an indispensable requirement for the conservation of life. This requires the constant functioning of properly conducted pharmacies manned by capable and well trained pharmacists.

Apothecaries' Profit

The price of the prescription to the patient has always included these services. Adam Smith, the famed eighteenth century British economist, in his treatise on "The Wealth of Nations" put it this way:

> Apothecaries profit is become a byeword, denoting something uncommonly extravagant. This great apparent profit, however, is frequently no more than the reasonable wages of labour. The skill of an apothecary is a much nicer and more delicate matter than that of any artificer whatever; and the trust which is reposed in him is of much greater importance. He is the physician of the poor in all cases, and of the rich when the distress or danger is not very great. His reward, therefore, ought to be suitable to his skill and his trust, and it arises generally from the price at which he sells his drugs. But the whole drugs which the best employed apothecary, in a large market town, will sell in a year, may not perhaps cost him above thirty or forty pounds. Though he should sell them, therefore, for three or four hundred, or at a thousand per cent profit, this may frequently be no more than the reasonable wages of his labour charged, in the only way in which he can charge them, upon the price of his drugs. The greater part of the apparent profit is real wages disguised in the garb of profit.

Emerging Roles

At the time when physicians' prescriptions, because of their frequent incompatibilities, require special compounding skills, the formal education of pharmacists was comparatively meager. Now that the compounding function has been transferred very largely to the manufacturer, the formal education of the practicing pharmacist has taken on not only a highly scientific character but an academic status which trains him for an appreciation of the chemistry, pharmacology, and therapeutic application of the products he dispenses. But the legal limitations on the practice of pharmacy are such as to restrict him in the application of his knowledge directly to the patient.

As a matter of fact, however, the revolution sometimes referred to in the prescribing and dispensing of drugs could really bring the pharmacist into his own professional domain as an adviser to the physician with respect to the composition, actions, contraindications, and dosage of the constantly developing new drugs.

The product of the lengthened pharmacy course should be qualified to become the super-detailman who can not only "detail" one manufacturer's products, but all prescription products, if he keeps himself properly informed. And while his fee for services must probably continue to come out of the charge made for the delivered prescription, the savings in manufacturers' promotional costs could offset this, while also meeting the physician's complaint about too much literature and too many detail men to see.

The pharmacist's role in acting as the adviser and guide to the public in their selection of drugs for self-medication, and counseling against this practice when it does not seem to be in the interest of the prospective buyer, should also be emphasized in connection with the sale of non-prescription drugs.

Hospital Pharmacists on the Job

Insofar as the hospital pharmacist is concerned, the Kefauver inquiry has not placed him on the spot to any considerable degree so far, but he should be alert to what is transpiring in the broad field of medical care. As the practices of the industry and the advantages generally provided to hospitals in reduced costs for drugs are being revealed in the Kefauver Committee hearings, references have been made from time to time by various witnesses to the formulary system; to prescribing by generic names; and to limiting the use of brand names in hospital prescribing practices. The hospital pharmacist enjoys the unique privilege of carrying on his work in the same institution as the physician who prescribes for the hospitalized patient. He is in constant communication with interns, residents, nurses, and staff physicians, and they have prompt and adequate access to him, so that any medication problem can be discussed interprofessionally and in person, "on the job." There is no question about the function performed by the hospital pharmacist or the necessity for his services now or in the future.

What has been brought out so far in these hearings is bound to have some effect on the practice of pharmacy in general. Every segment of the profession and the industry should be alert to the possibilities inherent in the recommendations which may result from the committee's study of the facts presented.

Whether legislation will be recommended or whether some agency will be set up, either governmental or voluntary, to endeavor to meet the public reaction to what are considered "high costs" of drugs will depend to a considerable extent on further evidence and information to be developed by the committee within the next several months.

In the meantime it behooves hospital pharmacists, as well as those engaged in retail prescription practice and the drug industry, to think constructively about ways and means of meeting the problems which have been brought to light.

► THE PRESCRIPTION DRUG INDUSTRY, IN REPLY to statements made to the Kefauver Committee, has disclosed a nine-point study program of national health needs and how to meet them.

Austin Smith, M.D., president of the Pharmaceutical Manufacturers Association, testifying (late in February) before a Senate subcommittee probing the drug industry, termed the program "another indication of the pharmaceutical industry's deep awareness of its obligations as a good citizen as well as good businessman."

PMA, in less than its two years' existence, already has formed more than sixty committees cooperating with government and private authorities in the health and drug fields. The organization's additional "good citizen" program, as announced by Dr. Smith, will include:

1. An expert committee to study and report continuously on trends and influencing factors in medical care costs as related to drugs.

2. A study of how PMA can undertake a "seeding" program to interest scholars in medical economics, similar to its established program with regard to clinical pharmacologists.

3. Examination of what educational program may be undertaken to prevent accidents befalling children who find carelessly placed drugs.

4. Determination of ways PMA can encourage more persons to enter every phase of the short-handed medical care field.

5. Study of how, by example, PMA can encourage teaching of physicians from less well developed areas in uses of drugs in patients, where hospitals and adequate treatment facilities may not be available.

6. Development of methods of continuous appraisal of areas of disease and discomfort, to help PMA member companies increase their efforts to bring relief from suffering and disease.

7. Appointment of a special committee from the drug industry to meet with other groups to study relationships of prescription needs to other medical care needs of the indigent and elderly. This would attack what Dr. Smith calls "a social problem that reflects wants extending far beyond the narrow boundaries set by prescription drug needs."

8. Continuing study of the role of drugs in domiciliary care of patients to ease hospital burdens.

9. Study of the role of drugs in special situations, such as driving, rehabilitation or accident-prone persons.

Therapeutic Trends

edited by WILLIAM JOHNSON

Guanethidine—A Hypotensive Agent

Twenty-five patients have been treated with guanethidine (2-per-hydroazocin-1'-ylethylguanidinium sulfate) in oral medication form for three to eleven weeks. Six of these patients received hydrochlorothiazide in addition. The results of this clinical study by Leishman *et al* appear in *Lancet II*:1044 (Dec. 12) 1959. The blood pressure fell in all but one of the patients. The hypotensive effect is long-continued and predominantly postural. In 18 cases the blood pressure is now considered to be satisfactorily controlled. Early in this trial it was noted that doses of 60 mg. daily produced severe hypotension and side effects, but recent experience has indicated that dosage of this order will seldom be required. Side effects ceased to be troublesome when treatment was started with 10 or 20 mg. guanethidine daily, the dose subsequently being increased by not more than 10 mg. at weekly intervals. It is indicated that the dosage of guanethidine must be individualized, depending on patient response. Guanethidine is an effective hypotensive drug which reduces blood pressure by progressive stages. The hypotensive action appears to be due to selective blockade of the sympathetic nervous system. The drug is easily administered and this trial has shown that, with suitable precautions, it can be used in the treatment of hypertensive patients.

WILLIAM E. JOHNSON

Piperazinepentanol—New Ataractic Agent

The present study of piperazinepentanol was based on laboratory evidence that it had potent antidesoxyephedrine and anti-emetic activity in animals at doses which did not cause any circulatory, respiratory, hepatic, renal, or bone marrow toxicity, but had definite calming action without causing hypnosis. The response of 38 patients with psychoneuroses in an outpatient clinic to this compound, 4(O-(propylthio)-phenyl)-1-piperazine pentanol, was observed. An average well tolerated dose was 50 mg. three times daily as reported by H. Levy *et al* in *Current Therapeutic Research 1*:34 (Sept.) 1959. The drug appeared to be moderately effective in relieving symptoms of anxiety and conversion manifestations, as compared to placebo studies previously carried out. The occurrence of drowsiness and postural hypotension would appear to limit its usefulness, but its beneficial effects plus the apparent lack of serious toxicity would warrant further studies of this drug or potent analogs.

SYLVIA SCHMIDT

Anticholinergic Compound

Compound S-1-1236 (1-methyl-1,4,5,6,tetrahydro-2-pyrimidyl-methyl-cyclohexyl-phenyl-glycolate hydrochloride) possesses anticholinergic, antispasmodic and antisecretory properties. Lara and Corral in *Am. J. Gastroenterol. 32*:591 (Nov.) 1959 state that its action is both central and peripheric. The drug was tested with uropepsin to determine the peptic secretion which is measured in terms of P.U. (Peptic Unit). Anticholinergic S-1-1236 caused a decrease in P.U. in every case, having a general average of 41 percent when 50 mg. were administered and 44 percent after administering 25 mg. (approximate values). Side effects were not significant with 25 mg. a day, thus making this apparently the dose of choice. It is active by the oral route and is characterized by a long-lasting effect after its administration. It possesses a wide margin of safety and offers results similar to those obtained with Banthine or Pro-Banthine, being less toxic than they are. S-1-1236 was furnished by the medical department of Pfizer de Mexico.

SYLVIA SCHMIDT

Amino-Glutethimide For Chronic Psychotic Epileptics

A compound, a-(*p*-amino-phenyl)-a-ethyl glutarimide, was discovered to have a good anticonvulsant activity alone or in combination with other anticonvulsants without the sedative side effect. Thirty-eight patients were selected on the basis of the diagnosis "chronic brain syndrome associated with convulsive disorder with psychotic reaction." Each of the patients was receiving either phenobarbital or diphenylhydantoin alone, or in combination, previous to this study. Initially each patient was given either 125 mg. or 250 mg. of amino-glutethimide daily. This dosage was increased by this same amount every five days until a therapeutic level of the drug was reached of be-

tween 750—2,000 mg. daily. In the last five months of the study, as reported by Niswander and Karacan in *Am. J. Psychiatry 116*:260 (Sept.) 1959, grand mal seizures were reduced 25 to 35 percent compared to seizure frequently before the project began. Side effects of a macular rash and nausea occurred in four patients, but disappeared when the dosage was reduced. Drowsiness was not observed as a side effect. Amino-glutethimide was supplied as Elipten by Ciba Pharmaceutical Products, Inc.

SYLVIA SCHMIDT

Deladumone—Therapy For Decubitus Ulcers

The anabolic steroid combination, Deladumone, was administered to a series of 11 elderly, debilitated, psychotic patients in an attempt to control chronic decubitus skin lesions. It has been recognized recently that metabolic disturbances underlie the formation and chronic course of decubitus ulcers, and this has resulted in emphasis on therapy to correct these basic disturbances. When prolonged periods of complete bed rest are unavoidable, the shift in nitrogen balance with the increased loss of protein metabolites in the urine greatly diminishes the reparative potential of the tissues. Deladumone, which contains 90 mg. testosterone enanthate and 4 mg. estradiol valerate per ml., was administered intramuscularly to the patients as a single injection of one or two ml. every 3 to 4 weeks for periods ranging from 1 to 9 months. Evidence from this study indicated that Deladumone promoted healing of decubitus ulcers and prevented the formation of new lesions. The results obtained suggest a more extensive investigation of the effectiveness of this preparation in larger groups of elderly and/or debilitated patients with existing or latent decubitus ulcers. Deladumone was supplied by the Squibb Institute for Medical Research and the results written by W. Forster and A. Henderson in *Current Therapeutic Research 1*:97 (Nov.) 1959.

SYLVIA SCHMIDT

Captodiamine

Captodiamine was developed in Denmark and submitted to extensive tests. It was concluded that the drug is a "non-hypnotic stabilizer" because the overall effect was not only primarily to relieve the symptoms of tension, but to ameliorate the underlying emotional instability of tension states. The drug was able to relieve agitation or depression resulting from tension and improve the abilities to think and function. Sixty patients were used in the study. The drug was used adjunctively with tranquilizers, stimulants, electric shock therapy or psychotherapy. The patients were all hospitalized patients with an age range of 16 to 60 and an average hospital stay of eight years. Castner and Noble reported the use of the drug in *Dis. Nerv. System 20*:594 (Dec.) 1959. The action of captodiamine is moderate sedation. Seventy-five percent of the patients treated showed definite improvement and were either discharged from the hospital or are working at jobs in and out of the hospital. The drug, supplied as Suvren by Ayerst Laboratories, merits further study.

RICHARD H. HARRISON

Epoxypiperazine In The Treatment Of Lymphomas And Other Neoplasms

Diepoxides, as useful agents as cytotoxic alkylating agents, have been previously proved. Epoxypiperazine was synthesized and was shown to be active in animals. Miller *et al* did this study to report the effects of the drug in clinical use. Sixty patients with malignant lymphomas and other neoplastic diseases were treated in the study. Side effects were noted in fifty percent of the patients. The chief side effect seemed to be vomiting which was greatly reduced when the dose, 60 mg./Kg., was given in divided doses. Results of the study, as reported in *Cancer Research 19*:1204 (Dec.) 1959, showed that significant clinical improvement was seen in patients with Hodgkin's disease, lymphosarcoma, reticulum-cell sarcoma, and mycosis fungoides. The results were similar to what might have been expected from the use of other alkylating agents. The same precautions regarding depressant effects on the white blood cells and platelets prevail as with other alkylating agents. Epoxypiperazine given orally to dogs caused nausea and vomiting. Oral administration has not been clinically attempted yet. The drug was administered intravenously. The drug for this study was supplied by Eli Lilly and Company.

RICHARD H. HARRISON

Intravenous Infusions Of Fat Emulsion And Anemia

Kaley, *et al.* report in *Am. J. Clin. Nutrition 7*:652 (Nov.-Dec.) 1959 on Lipomul infusions. The subjects for this study were seven, apparently physically well, schizophrenic patients. The members of the group were given daily infusions of 500 ml. of Lipomul for a period of twenty-nine days. All of the subjects but one developed an anemia of the hypochromic or hypochromic-microcytic type. Weekly hematograms were performed on each patient. The correlated results seemed to indicate that although the increased serum volume due to the repeated infusions may have been a contributing factor, it primarily was not the cause of the resulting anemias. The infusions were well tolerated by all but two subjects who experienced only mild to moderate reactions three to seven days after the series was completed. The mechanism appears to be a block in the synthesis of hemoglobin due to a decrease in serum iron and total iron binding capacity of serum. Lipomul for this study was supplied by the Upjohn Company.

DALE R. HYDER

News

Durant Accepts Wisconsin Position

Winston J. Durant

Winston J. Durant has recently accepted a job appointment as assistant professor (hospital pharmacy) in the School of Pharmacy at the University of Wisconsin and as Chief Pharmacist at University Hospitals in Madison. In announcing the appointment, Dean Arthur Uhl referred "to the necessity of developing this important area of hospital pharmacy in the curriculum of the School of Pharmacy, especially in view of the five-year pharmacy curriculum in 1960."

An honor graduate of the University of Colorado College of Pharmacy in 1950, Mr. Durant has also done graduate work in personnel management and accounting at the University of Chicago School of Business. He is a registered pharmacist in the states of Colorado, Illinois, and Nebraska. Immediately after graduation, Mr. Durant served for two years as a medical representative for E. R. Squibb and Sons, in Nebraska, followed by a year and a half of experience in a professional pharmacy.

In 1954 Mr. Durant became chief pharmacist at the University of Nebraska College of Medicine. This position offered him the opportunity of developing a formulary in cooperation with the Pharmacy and Therapeutics Committee; designing and remodeling the pharmacy department; streamlining methods of dispensing medication; as well as lecturing to junior medical students.

Mr. Durant left Nebraska to become Assistant Chief Pharmacist at the University of Chicago Clinics. This department then had seventeen registered pharmacists and nine pharmacy helpers He was in charge of the dispensary which filled over 700 individual prescriptions daily. He also carried the responsibility for some personnel matters.

Mr. Durant has held numerous other positions in hospital pharmacy and has participated in various hospital pharmacy projects. He is engaged on a part-time basis by the American Hospital Association to write a "Manual on Hospital Pharmacy." (This is a joint project of the A.H.A. and the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS.) For the past several years he has also been a member of the faculty for the annual institutes on hospital pharmacy conducted by the American Hospital Association in cooperation with the A.Ph.A. and ASHP.

Before leaving Nebraska, Mr. Durant was president-elect of the Nebraska Society of Hospital Pharmacists, and later became president of the Illinois Society of Hospital Pharmacists.

National Pharmacy Week Winners Named

Winners in the Hospitals and Clinics competition for the 1959 Display Contest during observance of National Pharmacy Week have been announced, along with winners in the other categories including retail pharmacy, public exhibits, and pharmacy colleges. National Pharmacy Week is sponsored annually by the American Pharmaceutical Association.

Sister M. Marysia, O.S.F., St. Francis Hospital, Litchfield, Illinois, was recipient of the first prize in the Hospitals and Clinics competition. The second prize is awarded to Benjamin Kaufman, Chief Pharmacist, Beth Israel Hospital, New York, N.Y.

Details and photographs of prize winning exhiits are included in the February issue of the *Journal of the American Pharmaceutical Association, Practical Pharmacy Edition.*

All entries in the national contest were judged by the Committee on Public Relations, headed by J. Warren Lansdowne, along with William S. Apple, George F. Archambault, John T. Fay, John A. Lynch, and Arthur N. Sorenson.

All national winners will receive their awards at the annual A.Ph.A. meeting in Washington, D.C., the week of August 14, and arrangements will be made by the state pharmaceutical associations for the presentation of the A.Ph.A. certificates to the state winners.

► THE SENIOR CLASS of the College of Pharmacy at the University of Minnesota visited facilities at Rochester, Minnesota on January 14, 1960. The class toured the hospital pharmacies at Rochester Methodist and St. Mary's Hospitals, the Special Observation Unit at Rochester Methodist Hospital, Weber and Judd Clinic Pharmacy, the Mayo Clinic with special emphasis on the Radioisotope Laboratory, and the Emergency Room, Poison Control Center, and patient floors at St. Mary's Hospital. The group was entertained at a noon luncheon at the Kahler Hotel at which time a panel discussed "The Role of a Pharmacy in a Hospital." Local arrangements were in charge of Earl Schwerman and Neal Schwartau of the Rochester Methodist Hospital Pharmacy.

► CHARLES M. KING, Chief of Pharmaceutical Service at the U. S. Public Health Service in Shawnee, Oklahoma, has recently been named Recording Secretary of the Potter County Pharmaceutical Association, Potter County, Shawnee. Mr. King completed the residency program at the Jefferson Medical College Hospital in Philadelphia in 1958. He is currently serving as Chairman of the SOCIETY's Special Committee on Classification and Filing Systems for Hospital Pharmacy.

► A POISON INFORMATION SERVICE has been instituted at the College of Pharmacy of the University of Rhode Island to serve as an ancillary service and liaison with the recently established Rhode Island Poison Control Center at Rhode Island Hospital in Providence. The service is under the direction of Dean Heber W. Youngken, Jr. of the College of Pharmacy.

IPSF Announces 1960 Study Tour

The International Pharmaceutical Students' Federation invites you to attend its 1960 Study Tour to be held this year in Stockholm, Sweden, from the 11 through 20 of August.

Included in this year's program are a bus and boat tour of Stockholm; visits to local pharmacies and the Royal Farmaceutical Institut; an all day trip to the old university-city of Uppsala; a boat trip in the Archipelago of Stockholm with music and dance; an all day tour to the castle and theatre of Drottningholm ended with a trip to Vallingby, the exceptional modern suburb of Stockholm; a tour of a Swedish pharmaceutical manufacturing plant; dinners; dances; church services; a symposium; and ample free time for souvenir hunting and private sightseeing. The all inclusive charge for the full nine days is only $39.90.

To facilitate planning, the Study Tour Committee of the IPSF has limited the number of applicants to be accepted from each country at twenty-five—this is a reason for early decision. Those interested should send a letter of application, no later than April 1, to:

Carl L. Vitalie
U.S. Liaison Secretary to IPSF
2630 Severance Street
Los Angeles 7, California

At time of application it is necessary to include a deposit of $13.50. Checks and money orders should be payable to: Carl L. Vitalie c/s 1960 IPSF Study Tour.

This Study Tour provides an excellent opportunity for Americans to meet and exchange ideas with fellow pharmacists and students from all over the world. All young pharmacists and pharmacy students who will be in Europe this summer are urged to include this Study Tour in their plans.

► JOSEPH J. HONICK, of Washington, D.C., has been appointed Special Assistant to Dr. William S. Apple, Secretary of the American Pharmaceutical Association, effective January 15. Before assuming his new position, Mr. Honick was on the editorial staff of *F-D-C Reports* and, for several years, served on the management staff of the U. S. Chamber of Commerce.

In his capacity with the American Pharmaceutical Association, Mr. Honick will assist Dr. Apple in the development of special projects assigned to the Office of the Secretary.

► GILBERT COLINA, Chief Pharmacist of Mercy Hospital, Charlotte, N.C. was recently presented with a ten year service pin by Mother Raphael, Administrator. The pin was given in recognition of his ten years' continuous service at the Mercy Hospital Pharmacy. Mr. Colina is active in the field of hospital pharmacy and is currently serving as President of the Southeastern Society of Hospital Pharmacists.

► WILLIAM BRINER has recently been named Chief of the Radiopharmaceutical Service of the Pharmacy Department at the Clinical Center of the National Institutes of Health, Bethesda. This is a new Service which has recently been established as part of the Pharmacy Department at the Clinical Center. In accordance with recent changes, the Pharmacy Department now includes the office of the Chief Pharmacist, Pharmaceutical and Development Service, Central Sterile Supply Service, and Radiopharmaceutical Service.

Mr. Briner is well known to members of the ASHP and is currently serving as Chairman of the SOCIETY's Committee on Radiopharmaceuticals.

► THE BRITISH PHARMACEUTICAL CONFERENCE will hold its 97th Annual Meeting at Newcastle upon Tyne (England), during the week commencing September 5, at which original scientific papers connected with pharmacy will be presented. All interested in pharmacy are invited to attend this Conference, particulars of which may be obtained from the address given below. Authors are invited to submit papers and a copy of the rules governing their presentation may be obtained from the Secretaries. The closing date for the submission of manuscripts is 23rd May, 1960. Full particulars may be obtained from the Honorary General Secretaries, British Pharmaceutical Conference, 17 Bloomsbury Square, London, W.C.1., England.

► DR. GLENN SONNEDECKER, Associate Professor (History of Pharmacy), School of Pharmacy, University of Wisconsin, and Director, American Institute of the History of Pharmacy, participated in Third Annual Visit-

News

Greater New York Hospital Association representatives at the Fifth Annual Luncheon of the National Pharmaceutical Council are shown with Dr. Austin Smith, President of the Pharmaceutical Manufacturers' Association and Newell Stewart, NPC Executive Vice President. Shown in photograph are (l. to r.) Mr. Stewart; Norman N. Baker, Apothecary in Chief, New York Hospital; Dr. Smith; Dr. August H. Groeschel, Associate Director of New York Hospital; and Dr. John V. Connorton, Executive Director of the Greater New York Hospital Association

ing Lecturer Series in the Pharmaceutical Sciences conducted by the University of Texas College of Pharmacy during the spring term. Dr. Sonnedecker, speaking at the February 9 and 10 Seminars, covered the following subjects: "To Be, or Not To Be—Professional;" "The Artist and the Pharmacist;" and "Health Insurance as an International Trend Affecting Pharmacy."

► Dr. W. Arthur Purdum, has recently accepted a new position as Vice-President in charge of production and new product development at Burrough Brothers Manufacturing Company, a Baltimore pharmaceutical establishment which has been in business since 1863. Dr. Purdum is well known to hospital pharmacists and is a past-president of the American Society of Hospital Pharmacists. He is also affiliated with the University of Maryland where he teaches courses in hospital pharmacy.

Purdue Offers Radioisotopes Course

A two-day symposium on the use of radioisotopes in the pharmaceutical and allied industries, to be followed by a four-weeks course, will be offered at Purdue University. The program is being planned by the Bionucleonics Department of the University with the cooperation of the Office of Isotopes Development of the U. S. Atomic Energy Commission.

The symposium will be held on April 25-26. Speakers will cover not only present and future applications of radioisotopes, but also public health problems. The course, which is designed to acquaint technical personnel with radioisotopes in order that they may use them safely and efficiently in pharmaceutical research, control and production, will continue through May 20.

"Public Health and Welfare as It Relates to the Food Additive Problem," an important topic relating to recent discussions of the contamination of foods, will be discussed by one of the foremost authorities in this field, Arnold J. Lehman, director of the Division of Pharmacology, Bureau of Biological and Physical Sciences of the Food and Drug Administration, Washington, D. C. Lehman will speak following a banquet on Monday evening, April 25.

Two representatives of the Atomic Energy Commission will appear on the program for the symposium. Oscar M. Bizzell, Chief of the Isotopes Applications Branch, will discuss "General Industrial Applications of Radioisotopes," and Joseph E. Machurek, Chief of the Radiation Branch, will discuss "Industrial Applications of High Level Irradiation Sources to Industry."

Further discussions on the applications of radioisotopes will be given by J. F. Snell, Pfizer Therapeutic Institute, Maywood, N. J., on "The Applications of Radioisotopes to Trace Level Research Including Residue and Metabolite Studies"; Benjamin F. Scott, Nuclear-Chicago Corporation, Chicago, "Analytical Applications of Radioisotopes, Present and Future"; and George B. Foster, Foster Engineering Corporation, Columbus, Ohio, "The Uses of Radioisotopes in Production Problems and Technical Operations."

Relating to the safe and efficient use of radioisotopes, Phillip Shevick, also of the Nuclear-Chicago Corporation, will speak on "Radioisotope Laboratory Design, Instruments, and Cost," and W. Van Winkle, Jr., Ethicon, Inc., Somerville, N. J., on "Radiation Sterilization in the Pharmaceutical and Allied Industries." Stephen P. Cobb, National Association of Manufacturers, New York, will discuss "Why Radioisotopes—Management's Technical and Economic Evaluation."

Professor John E. Christian, head of the Bionucleonics Department at Purdue, is to open the meeting with a talk on "Principles, Methods, and Areas of Usefulness of Radioactivity in Pharmaceutical Research, Control and Production." Other members of the Purdue staff who will appear on the program to discuss various applications of radioisotopes and radiation safety are B. G. Dunavant, Assistant Professor of Health Physics; William F. Bousquet, Assistant Professor of Bionucleonics; and Paul L. Ziemer, Radiological Control Officer.

The two-day symposium is open to all technical and management people interested in the application of radioisotopes, but the four-week course will be limited to a maximum enrollment of 24 persons, Professor Christian has announced.

Maryland Hospital Pharmacy Residency

The University of Maryland School of Pharmacy and University Hospital, announce the combined Graduate Study-Residency Program in Hospital Pharmacy starting September 1, 1960. Upon satisfactory completion of the program, the Master of Science degree will be conferred by the University of Maryland and a Certificate of Residency in Hospital Pharmacy will be awarded by the Hospital.

Appointments to the residency are for a period of 22 months beginning September 1, 1960. During the academic school year, the resident will devote one-half of his time to the hospital pharmacy training and one-half of his time to graduate study at the School of Pharmacy. Full-time training in the University Hospital Pharmacy will be required during the summer session of 1961. The University Hospital will provide a stipend of $266.66 per month, parking space, uniforms and laundry of uniforms without charge. Blue Cross or other acceptable hospitalization insurance must be carried by the resident and is available under the payroll deduction plan of the University.

Applicants must be graduates of accredited colleges or schools of pharmacy and be able to meet the requirements for admission to the graduate school of the University of Maryland. There is no formal application blank for this program. Applicants will be required to submit a statement giving full details as to date and place of birth, citizenship, health, marital status, education and pharmaceutical experience along with a small recent photograph. Also required is an official transcript of undergraduate work completed to date. The applicant should ask the Dean and two other members of his college faculty to write to the Director of University Hospital regarding the applicant's personality and fitness. Deadline for letters of application and other required information is April 1, 1960. All applicants will be notified as of May 1, 1960.

The material requested above should be addressed to Mr. Lad F. Grapski, Director, University Hospital, University of Maryland, Baltimore 1, Maryland.

University of Arkansas Medical Center Hospital Pharmacy Internships — Residencies

The University of Arkansas Medical Center is again offering Internships and Residencies in Hospital Pharmacy. Designed to meet the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS' Minimum Standard for Pharmacy Internships in Hospitals, the training includes experience in outpatient dispensing, inpatient dispensing, bulk compounding of both sterile and nonsterile products, and hospital pharmacy management.

Applications for the year beginning 1 July 1960, should be filed before 15 April 1960. Applicants for the Residencies must have a B.S. degree in pharmacy and be registered pharmacists in one of the United States. Applicants for the Internships must have a B.S. degree in Pharmacy, but need not be registered. Undergraduates may apply before being graduated but must submit proof of graduation before they can be appointed.

A Certificate of Residency in Hospital Pharmacy or a Certificate of Internship in Hospital Pharmacy is awarded by the University Hospital on completion of the respective programs. Interns and Residents receive a stipend of $400 per month during the one-year program.

Applicants who qualify for admission to the Graduate School may serve their Internship or Residency on a half-time basis while taking graduate work toward the M.S. or Ph.D. in the graduate program of the School of Medicine. Majors for the M.S. are available in the fields of biochemistry, pharmacology, physiology, microbiology, and anatomy and for the Ph.D. in biochemistry and pharmacology. For half-time Interns or Residents, the stipend is $200 per month.

Additional information and application blanks may be obtained from the chief pharmacist, William M. Heller, Ph.D., University of Arkansas Medical Center, Little Rock, Arkansas.

The Johns Hopkins Hospital Internship

The Johns Hopkins Hospital, in cooperation with the Graduate School and the School of Pharmacy of the University of Maryland, announce that internships in pharmacy are open to a limited number of 1960 or other recent graduates of recognized schools of pharmacy. Appointments are for a period of twenty-two months beginning September 1, 1960. During twenty months interns devote one-half time to hospital pharmacy training and one-half to graduate study. Full time training in the hospital pharmacy is required for two months during the summer of 1961. Four weeks of vacation are allowed during the term of appointment. Upon satisfactory completion of the internship and the course of study, Master of Science degrees are conferred by the University of Maryland and Certificates of Internship are awarded by The Johns Hopkins Hospital.

A stipend of $200.00 per month is provided by the hospital. The University of Maryland makes a reduction of 25% in tuition fees. The full graduate tuition is $12.00 per semester hour and thirty semester hours of work are required for the Master's Degree. In addition, there is a $10.00 matriculation fee, a $10.00 diploma fee and student union building fee. Information regarding curricula appears in the catalog of the School of Pharmacy, a copy of which may be secured by sending a request to the School of Pharmacy, University of Maryland, 636 West Lombard Street, Baltimore 1, Md.

Opportunity is offered for well-rounded practical experience in hospital pharmacy administration, pharmaceutical manufacturing, prescription compounding, dispensing, and in the preparation of sterile solutions and other sterile products. The facilities of the Welch Medical Library of The Johns Hopkins University and the libraries of the University of Maryland are available. Off duty hours are so arranged that one intern is on call to take care of emergency orders when the hospital pharmacy is closed. During the term of appointment, interns may be invited to attend, at hospital expense, meetings and conventions conducted in this area of the country. Interns may live at the hospital or, if they prefer, they may rent nearby rooms or apartments. Rooms in the hospital residence rent for $40.00 per month. Meals may be purchased for a nominal sum in the hospital dining rooms.

Regulations regarding the personal conduct and habits are those established by the Director of the Hospital for interns on other hospital services. There is no formal application blank under this program. Applicants must submit a statement giving full details as to date and place of birth, citizenship, health, marital status, education and pharmaceutical experience together with a small recent photograph. An official transcript of the applicant's college record and letters from the dean and two other members of the faculty of his college are to be sent to the Director giving their estimates of the applicant's personality and fitness.

Letters of application and other required information should be forwarded to Russell A. Nelson, M. D., Director, The Johns Hopkins Hospital, Baltimore 5, Maryland, not later than April 1 and appointments will be announced on or before May 1, 1960.

SELECTED PHARMACEUTICAL ABSTRACTS

and summaries of other articles interesting to hospital pharmacists

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edited by CLIFTON J. LATIOLAIS, HENRY J. DEREWICZ *and* LEO F. GODLEY

HYDROLYSIS OF NAPHAZOLINE

Kinetics of the Specific Base-Catalyzed Hydrolysis of Naphazoline, Stern, M. J., King, L. D., and Marcus, A. D., J. Am. Pharm. Assoc., Sci. Ed. 48:641 (Nov.) 1959. (College of Pharmacy, Rutgers University, Newark 4, N. J.)

The rate of the specific base-catalyzed hydrolysis of naphazoline has been found to be first order with respect to both naphazoline and hydroxyl ion, regardless of whether the naphazoline exists as the protonated or unprotonated species. A theoretical isothermal equation expressing the pseudo-first order specific rate constant as a function of the hydronium ion and hydroxyl ion activities has been derived, and at 25° appears to hold true over a 10 million-fold variation in catalyst (hydroxyl ion) concentration. The activation energies and frequency factors for both the hydrolyses of protonated naphazoline and unprotonated naphazoline have been experimentally determined. The reaction involving protonated naphazoline is favored by frequency while the reaction involving unprotonated naphazoline is favored by energy. The frequency effect is the greater so that, at normal temperatures, protonated naphazoline hydrolyzes about 1000 times faster than the unprotonated form. Postulations for the mechanisms of the reactions have been made in light of the kinetic data and a generalized equation for calculating the observed rate constant has been devised.

AUTHOR'S SUMMARY

STERILIZATION OF SPORES

Ethylene Oxide Sterilization of Spores in Hygroscopic Environments, Opfell, J. B., Hohmann, J. P., and Latham, A. B., J. Am. Pharm. Assoc., Sci. Ed. 48:617 (Nov.) 1959. (Cutter Laboratories, Berkeley 10, Calif.)

The effect of inoculating objects to be sterilized on the evaluation of the sterilization process was studied. The results of this study suggest a possible explanation for the contradictory observations. As the test organism, spores of *Bacillus subtilis* strain *B. globigii* were used in the experiment. They were exposed to ethylene oxide after being dried on several types of surfaces. Results proved glycerin or filter paper in immediate contact with dried *B. globigii* spores to be significantly effective in reducing the spores' resistance to ethylene oxide exposure.

H. A. K. WHITNEY, JR.

VITAMIN A DETERMINATION

A Simplified Procedure for the Determination of Vitamin A, Napoli, J. A., Senkowski, B. Z., and Motchane, A. E., J. Am. Pharm. Assoc., Sci. Ed. 48:611 (Nov.) 1959. (Control Spectrophotometric and Physical Chemistry Laboratories of Hoffmann-La Roche Inc., Nutley, N. J.)

An improvement of the U.S.P. XV procedure for the quantitative analysis of vitamin A is described. The improvement proposed consists of the use of a single extraction in place of the multiple extractions of the U.S.P. procedure. Replacement of the 4 ether extractions called for in the U.S.P. XV procedure for vitamin A determination by one extraction with a five-fold volume of ether results in a partial, but significant, improvement in operation and results. Notably, two things are achieved: the time of analysis is reduced to almost one-half, and the precision of the absorption measured is increased two to three times. The precision of the Morton-Stubbs correction factor remains unchanged. The method is shown to be applicable to a wide range of products. The description of the procedure includes sampling technic, saponification, extraction, washing technic, and measurement of absorbance. A discussion of solvent purification and instrument checking and calibration is included. Several series of comparisons are presented between results obtained by the new method and by the U.S.P. XV.

H. A. K. WHITNEY, JR.

INJECTABLE SOLUTIONS

Osmotic Concentration and Osmotic Pressure in Injectable Solutions, Setnikar, I. and Temelcou, O., J. Am. Pharm. Assoc., Sci. Ed. 48:628 (Nov.) 1959. (Research Department, Recordati Laboratorio Farmacologico S. p. A., Milano, Italy.)

A search for a method of direct determination of isotonic concentration was made and it has been found that this could be done fairly simply by means of a suitable modification of the hematocrit method. This paper describes the method employed and the results obtained therefrom. Human and rabbit blood were drawn. The blood samples were centrifuged, the separated red cells were added to an equal volume of the solution under examination, and this suspension was centrifuged for 30 minutes at 3000 r.p.m. in Wintrobe's hematocrit tubes. To determine the volume that the red cells would maintain in an isotonic solution, a similar test was performed mixing the red cells with the plasma of the same specimen of blood. Varying concentrations of the following solutions were used: sodium chloride, urea, dextrose, procaine hydrochloride, saponin, and zinc sulfate. Similar experiments carried out on substances of pharmaceutical interest showed that they can be classified into different groups according to their diffusibility through the erythrocyte membrane and their action upon it. It was demonstrated *in vitro* and *in vivo* that for many substances the iso-osmotic concentration is not equivalent to the isotonic concentration and that the confusion between iso-osmia and isotonia can have dangerous consequences.

H. A. K. WHITNEY, JR.

TESTING OF GLASS AMPULS AND TUBES

Increasing the Precision of the Testing of Chemical Stability of Glass Ampuls and Tubes, Bril, I.L., Solomina, E.P., and Soloviyeva, O. A., Meditsinskaya Promyshlennost SSSR (U.S.S.R.) 13, 11 : 26 (Nov.) 1959.

The usual method for testing the chemical stability of glass material utilized in the production of glass ampuls and tubes for injectable solutions consists in filling these containers with an acid solution of methyl red and subsequent autoclaving at 2 atmospheres during 30 minutes. Afterwards the yellow color of the ampuled liquid is an indication of poor stability of glass. However, as the visual assessing of the color of the indicator is often very difficult the authors suggest the use of standard solutions with which the color of the autoclaved liquid is to be compared. Alternatively, the colorimetric determination of optical density may serve as an index of the chemical stability. The standard solution for comparative purposes is to be prepared by adding 0.05-0.11 ml. 0.05 N sodium hydroxide solution (according to the glass tested) to 10 ml. solution of methyl red. When testing the chemical stability of the glass colorimetrically, the minimum allowable optical density of autoclaved solution of methyl red proved to be 0.04. The determination is to be effected by taking the sample of the autoclaved liquid in the amount of 1.4 ml. and measuring in a cuvette with a working thickness of 3 mm.

HUBERT ŽÁČEK

PREPARATION OF EXTRACT FROM MARSHMALLOW ROOT

Improving the Process of Preparation of Extract from Marshmallow Root, Gontsharenko, G.K., and Ignatiyenko, A.G., Meditsinskaya Promyshlennost SSSR (U.S.S.R.) 13, 7 : 49 (July) 1959. (Chimico-Pharmaceutical Research Institute, Kharkov, U.S.S.R.)

The following recommendations based upon results of experiments are given for the purpose of improving the usual method of preparation of extract from *Radix althaeae*: (1) The root is to be macerated during not more than 2 - 2½ hours while stirring by means of a mechanical shovel-like stirrer (30-40 turn/min.). (2) The separation of extract from the residue is to be realized by means of a sieve with openings of 1-0.5 mm. At the end of the pressing process, vacuum (300-400 mm. mercury) is to be used. (3) After 1 hour of sedimentation the extract is to be treated by decantation and filtered in vacuum (300 - 400 mm. mercury) through linen.

HUBERT ŽÁČEK

PHARMACEUTICAL EDUCATION IN THE U.S.S.R.

Development of Higher Pharmaceutical Education in the U.S.S.R. in the Postwar Years, Sidorkov, A.M., Aptechnoe Delo (U.S.S.R.) 8, 6 : 44 (Nov.-Dec.) 1959.

At this time there are in the U.S.S.R. 6 pharmaceutical institutes (Leningrad, Perm, Piyatigorsk, Zaporoshe, Kharkov, and Tashkent), 10 pharmaceutical faculties as parts of medical institutes (Alma-Ata, Baku, Irkutsk, Dniyepropetrovsk, Kaunas, Riga, Lvov, Moscow, Tbilisi, and Tomsk), and 1 pharmaceutical department as part of a medical faculty (Tartu). At the beginning of the year 1956/1957 there were 9,100 students attending the above mentioned schools; whereas at the beginning of 1945/46 there were in the U.S.S.R. 6,000 students of pharmacy only. Formerly the duration of the study was 4 years; beginning with 1949/50 it was lengthened to 5 years. The qualification of the teaching personnel is very good.

HUBERT ŽÁČEK

VARIATIONS IN ISOTONICITY

Isotonic Solutions VIII, The Permeability of Red Corpuscles to Various Salts of Gluconic Acid, Ansel, H.C., Husa, W.J., J. Am. Pharm. Assoc., Sci. Ed. 48:516 (Sept.) 1959. (College of Pharmacy, University of Florida, Gainesville.)

A comparison was made of van't Hoff *i* values calculated from hemolytic and freezing point data for various salts of gluconic acid. Sodium, potassium, and manganese (II) gluconates gave higher *i* values by the hemolytic method than by the freezing point depression method; iron(II) and cobalt(II) gluconates gave lower *i* values by the hemolytic method. Magnesium and calcium gluconates gave higher *i* values by the hemolytic method with human erythrocytes but not with rabbit erythrocytes. Zinc gluconate gave extremely high hemolytic *i* values due to partial precipitation of the oxyhemoglobin liberated from laked erythrocytes. Hemolytic *i* values of the gluconates were generally lowered when determined in the presence of sodium chloride. Erythrocytes from Negro donors were, on the average, more resistant to osmotic hemolysis than those from Caucasian donors. Results substantiate the premise that solutions calculated to be iso-osmotic with blood according to colligative property data are not necessarily isotonic to the red corpuscle.

AUTHOR'S SUMMARY

EXTRACTION OF ALKALOIDS

A Note on the Use of Citric Acid and Tartaric Acid Buffers in the Extraction of Solanaceous Alkaloids by Centrifugation, Tsas, D.P.N., J. Am. Pharm. Assoc., Sci. Ed. 48:548 (Sept.) 1959. (College of Pharmacy, University of Rhode Island, Kingston.)

This note describes a modified method for the Witt procedure of extraction of solanaceous alkaloids. This modification is the substitution of centrifugation for filtration. Also studied are the effects of citric acid and tartaric acid buffers in the extraction process. The tartaric acid buffer proved slightly more efficient for the extraction of the alkaloids from the plants studied but the increase was not significant. The centrifugation method did not appreciably improve the yields but afforded a great saving in time over the filtration method.

WILLARD HARRISON

ANTIMICROBIAL PROPERTIES OF SALICYLANILIDES

Substituted Salicylanilides with Antimicrobial Activity, Taborsky, R.G., Darker, G.D., Kaye, S., J. Am. Pharm. Assoc., Sci. Ed. 48:503 (Sept.) 1959. (Ben Venue Laboratories, Inc., Bedford, Ohio.)

Since salicylanilide is widely used as a commercial fungistat, work was done on developing some derivatives of this compound which might possibly have a wider range of antimicrobial activity. Eighteen new halonitrosalicylanilides were developed. The synthesis was accomplished by three methods. Reaction of the respective dinitro or nitrosalicoyl chlorides with an excess of the halogenated aniline in benzene was found to be a satisfactory method which gave the halonitrosalicylanilides in 71-93% yields. Most of the salicylanilides in the present work were made by this method. However, interaction of the acid, the aniline, and phosphorous trichloride in benzene was also found to be useful. In a third method, a Schotten-Baumann reaction between the acid chloride and the aniline in the presence of aqueous sodium hydroxide gave low yields of the desired anilides which were highly contaminated by the acids.

Antibacterial screening revealed that the halo-3,5-dinitrosalicylanilides had little or no activity while the halo-3-nitro and the halo-5-nitrosalicylanilides showed potent activities against some types of bacteria and fungus. These results indicate that both the nitro and halogen groups confer antibacterial activity upon the salicylanilide parent molecule, which when unsubstituted exhibits very little antibacterial action. Further studies revealed that although the nitro and halogen substituents confer antibacterial properties upon the salicylanilide, they neither enhance nor lower its already high antifungal activity. Preliminary toxicity studies show that the halo-3-nitro-salicylanilides are consistently several times more toxic to rats than the halo-5-nitro isomers.

WILLARD HARRISON

ACRIFLAVINE IN EMULSION BASES

Thermosterilized Acriflavine Emulsion Ointment, Menczel, E., Grun, S., J. Am. Pharm. Assoc., Sci. Ed. 48:508 (Sept.) 1959. (Bacteriological Laboratory, Hadassah Hospital, Tel-Aviv, and the School of Pharmacy, Hebrew University, Jerusalem.)

Various acriflavine ointments are clinically used for topical antisepsis because they are not hindered by the resistance encountered with antibiotics and other bacteriostatic agents. The bacteriostatic activity of acriflavine ointments depends upon the ointment base as well as the concentration of acriflavine. It was found that the most effective formulation for an acriflavine ointment was a stable water-miscible emulsion base of high water content. However, another problem is one of sterilizing the ointment and thermostability is highly desirable. It was found that thermostable, sterilizable emulsions could be prepared by utilizing selected emulsifying agents properly blended. Polyoxyethylene 30 stearate, when mixed with auxiliary dispersion agents could produce thermosterilizable emulsion bases. From these bases 4 of proper consistency were selected for the preparation of sterile acriflavine ointments. The studies with these bases established that a 1% w/w concentration of acriflavine gave effective antiseptic action.

WILLARD HARRISON

DIGITALIS GLYCOSIDES

Enzymatic Decomposition of Digitalis Glycosides IV, Gisvold, O., J. Am. Pharm. Assoc., Sci. Ed. 48:532 (Sept.) 1959. (College of Pharmacy, University of Minnesota, Minneapolis.)

A study was made of the glycosides obtained from various species of digitalis. The extracts were made with both enzyme inhibiting and enzyme favoring conditions prevailing. Desglucoglycosides are obtained when enzymatic action is allowed while native glycosides are obtained when the enzymes are inhibited. Because 40% concentration of methanol did not inhibit enzyme activity whereas 66% did, these concentrations were used to

extract the dried leaves of some of the species. The use of 40% methanol to prepare primary extracts has certain advantages over water such as more complete extraction of the desglucoglycosides, much smaller volumes of solvent needed, easier filtration or percolation, and less troublesome emulsions with subsequent extractions. Disadvantages encountered were incomplete extraction of the native glycosides from the primary extract by other organic solvents, and considerably greater amounts of undesirable substances are extracted in the primary and subsequent extractions. Other solvent combinations were tried but they seemed to have nearly the same advantages and disadvantages.

WILLARD HARRISON

PREPARATION OF CASEIN HYDROLYSATES

The Reduction of Hydrolysis Time and Tryptophan Destruction in the Preparation of Casein Hydrolysates, Venturella, V.S., Sager, R.W., Bianculli, J.A., J. Am. Pharm. Assoc., Sci. Ed. 48:500 (Sept.) 1959. (School of Pharmacy, University of Pittsburgh, Pittsburgh 13, Pa.)

Lack of speed in preparation and the degree of tryptophan destruction exhibited by the commercial methods of preparing casein hydrolysates have led to the development of a modified method which reduces both the length of time required and the amount of tryptophan destruction. The method deals with allowing partial hydrolysis to occur by enzymatic action and then treating the substance with diluted acid to hydrolyze the polypeptide chains to the smaller peptides desired. The potential value of the method is that of possibly reducing the time required to produce the same degree of hydrolysis from 100 hours, as is required with the enzymatic digestion alone, to 17-22 hours, which is all the time needed with the new method. In addition it was found that this combination method showed less tryptophan destruction than is observed with the use of strong acid alone for the hydrolysis procedure. The main desirability of this combination enzyme-acid hydrolysis is the greater speed at which it can be accomplished with no greater tryptophan destruction than the longer enzymatic method.

WILLARD HARRISON

IMPROVED HYDROGEN PEROXIDE

Treatment of Pharyngitis and Laryngitis with an Improved Hydrogen Peroxide, Harkins, H.P., Eye, Ear, Nose, Throat Monthly 38:942 (Nov.) 1959.

Because of the increasing incidence of bacterial resistance and allergy to antibiotics, long established antibacterial agents are being re-evaluated for their usefulness in the treatment of topical diseases. As a result, hydrogen peroxide has been reconsidered for the following reasons: (1) It is a wide spectrum bactericide and is effective against some fungi. (2) It is nonallergenic, completely nontoxic, nonirritating and nonsensitizing.

The main disadvantage of the 3% aqueous solution of hydrogen peroxide is that it is very rapidly broken down by the catalase present in most body fluids so that its action is fleeting. However, it was found that a product (Gly-Oxide G.H.P.) containing 10% urea peroxide in glycerin remains stable and releases hydrogen peroxide over a long period of time when in contact with pharyngeal and laryngeal mucosa. This product was found to have special debriding and detergent action and was most effective in relieving the itching and burning which accompanies smoker's pharyngitis.

ROBERT L. RAVIN

IODOPHORS

Iodophors in Dermatology, Burdick, K.H., A.M.A. Arch. Derm. 80:587 (Nov.) 1959.

A new type of detergent-iodine complex of the "iodophor" group was used in treating primarily or secondarily infected skin diseases for a four-year period and was found to be effective over a wide range of infectious agents. The iodophor evaluated had the following composition:

Polyethoxy polypropoxy ethanol-iodine complex	7.75%
Nonylphenyl ether of polyethylene glycol-iodine complex	7.75%
Hydrogen chloride	0.10%
Inert material	84.40%

This detergent-iodine complex was found to have the following advantages over its older counterparts: (1) When properly used, it was found to be relatively free from toxicity, irritation, staining and odor. (2) It penetrated rapidly into fatty materials and was not rapidly bound to proteins. (3) It was stable under normal storage conditions and was water-soluble.

The following tabulation summarizes the clinical impression of this compound:

Excellent Results: (one-ounce-to-one-liter dilution)
- Kaposi's varicelliform eruption
- Secondary impetiginized dermatoses
- Mixed intertriginous infections
- Infectious eczematoid dermatitis
- Molluscum contagiosum

Very Good Results: (one-ounce-to-one-liter dilution)
- Herpes zoster
- Folliculitis
- Hidroadenitis suppurativa
- Dermatophytosis
- Monilial paronychias (Applied full strength)
- Onychomycosis (Applied full strength)
- Flat or juvenile warts (Applied full strength)

Satisfactory Results (one-ounce-to-one-liter dilution)
- Pustular bacterid
- Dermatitis repens
- Furunculosis

ROBERT L. RAVIN

CURRENT LITERATURE

. . . also calling your attention to the following articles appearing in recent hospital and pharmaceutical journals

. . . . . .

ADMINISTRATION

—Purchasing

Keheley, Lewis R.: Why a Written Policy is Basic to Good Purchasing Practice, *Hospitals* 34:71 (Feb. 16) 1960.

FORMULARY SYSTEM

Archambault, George F.: The Formulary System vs. the New Concept of 'Substitution,' *Hospitals* 34:71 (Feb. 1) 1960.

LIBRARY AND REFERENCE

Vance, Joe: Pharmacy from a Textbook, *Southern Hospitals 28*:52 (Feb.) 1950.

OUTPATIENT DISPENSING

Bowles, Grover C.: Distribution Patterns in Drugs in Hospitals, *Am. Profess. Pharm. 26*:126 (Feb.) 1960.

Moravec, Daniel F.: Hospital Outpatient Dispensing, *Hosp. Management* 89:80 (Mar. 1) 1960.

Sowinski, Rosemarie P.: Current Trends in Outpatient Pharmacy Service, *Am. Profess. Pharm. 26*:56 (Jan.) 1960.

RECRUITMENT

Holland, Madeline Oxford: Women in Hospital Pharmacy, *Am. Profess. Pharm. 25*:795 (Nov.) 1959.

GENERAL

Sister Mary John: Control of Staph Infections—A Challenge to the Pharmacist, *Am. Profess. Pharm. 25*:862 (Dec.) 1959.

Sperandio, Glen: The Pharmacist and Mental Health, *Tile and Till 46*:opp.8 (Jan.-Feb.) 1960.

DRUG EVALUATIONS

by the Council on Drugs of the American Medical Association

► THE FOLLOWING MONOGRAPHS and supplemental statements on drugs have been authorized by the Council on Drugs of the American Medical Association for publication and inclusion in *New and Nonofficial Drugs*. They are based upon the evaluation of available scientific data and reports of investigations.

The issues of the *Journal of the American Medical Association* from which each monograph has been taken is noted under each monograph. Monographs in this issue of the JOURNAL include those published in the *A.M.A. Journal* for December 12, 1959 and January 2, 1960.

Notice

New and Nonofficial Drugs 1960 is now available from your local bookstore and from the publishers, J. B. Lippincott Company, Philadelphia, Pa. This 1960 edition contains monographs of drugs evaluated by the Council on Drugs of the American Medical Association and published in the Journal of the A.M.A. to October 17, 1959. The indexes listed below contain those drugs evaluated and published between October 24, 1959 and January 2, 1960.

Index

TO DRUGS EVALUATED IN THIS ISSUE

Index

TO EVALUATED DRUGS AND ARTICLES IN THE FEBRUARY ISSUE OF THE AMERICAN JOURNAL OF HOSPITAL PHARMACY.

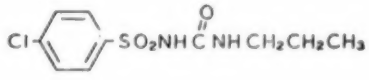
NEW AND NONOFFICIAL DRUGS

The following descriptions of drugs are based upon available evidence and do not in any case imply endorsement by the Council.

H. D. KAUTZ, M.D., *Secretary*

Chlorpropamide — Diabinese®

CHLOPROPAMIDE (Diabinese) is 1-propyl-3-(*p*-chlorophenyl) sulfonylurea.—The structural formula of chlorpropamide may be represented as follows:



Actions and Uses

Chlorpropamide, an arylsulfonylurea, is an orally active hypoglycemic agent which is used for the management of selected patients with diabetes mellitus. The pharmacological actions and clinical uses of chlorpropamide are essentially the same as those of the closely related compound, tolbutamide, and both drugs are believed to influence blood sugar levels by the same basic mechanism of action. (See the monograph on tolbutamide in New and Nonofficial Drugs.) Chlorpropamide is rapidly absorbed from the gastrointestinal tract; the drug is detectable in the blood within one hour after a single orally administered dose, and blood levels are maximal within two to four hours. Because it is excreted very slowly mostly in unchanged form by the kidney, blood levels of chlorpropamide are maintained for considerably longer periods of time than with tolbutamide. This persistence in the body results in a sustained hypoglycemic action. Consequently, doses one-fourth to one-half as great, given less frequently, will produce the same control of the blood sugar level. In this sense, chlorpropamide may be considered more potent than tolbutamide. This in itself should not be construed to indicate

that chlorpropamide is more effective. However, certain clinical evidence and laboratory determinations in the form of comparative blood sugar levels within four hours after single-dose administration is also available to indicate that, on an equivalent dose and blood level basis, chlorpropamide has a somewhat greater therapeutic effect than has tolbutamide. This enhanced pharmacological potency may be a factor, along with the delayed excretion, in the production of the desired therapeutic effect with lower, less frequently administered dosage.

Clinical experience with chlorpropamide is presently much less than with tolbutamide. Nevertheless, it is already apparent that both drugs have the same general usefulness. Thus, satisfactory control of the diabetic state with chlorpropamide can be anticipated chiefly in those patients with uncomplicated diabetes mellitus of the stable, nonketotic, maturity-onset or adult type which cannot be controlled by dietary restriction alone. Chlorpropamide may reduce the amount of insulin needed by some patients with juvenile or growth-onset type of diabetes, or unstable or "brittle" type of diabetes, thus permitting a more satisfactory 24-hour control of hyperglycemia than is possible with insulin alone. Like tolbutamide, it is of no value or is contraindicated in patients with diabetes complicated by ketosis, acidosis, diabetic coma, fever, severe trauma, gangrene, Raynaud's disease, or serious impairment of thyroid, renal, or hepatic function. The drug can be used successfully for controlling hyperglycemia in diabetic patients who initially or secondarily fail to respond to tolbutamide.

The criteria used to select candidates for therapy with chlorpropamide are the same as those set forth for tolbutamide. Therapy with chlorpropamide should be undertaken with the same caution as with tolbutamide. Careful instruction of the patient, insistence on rigid adherence to dietary restrictions, and meticulous follow-up observations—all essential for the safe and efficacious use of tolbutamide—are equally necessary with use of chlorpropamide.

In general, all of the side-effects and untoward reactions previously reported with tolbutamide have been observed with chlorpropamide. Although the over-all incidence of these effects is low, most investigators indicate that they tend to occur somewhat more frequently with chlorpropamide than with tolbutamide. It is to be noted, however, that average doses of chlorpropamide considerably in excess of those now recommended and found clinically effective were believed necessary in the early clinical investigations, and, as a result, the reported incidence of toxicity may be unduly high. The influence of lower dosage levels now being used to decrease the incidence of toxic effects remains to be seen. In addition, there is considerable evidence that all sulfonylurea compounds interfere, to some degree, with certain enzymatic processes within the liver; in this respect chlorpropamide is similar to tolbutamide in that both should be administered with extreme caution, if at all, to patients with a history of hepatic dysfunction, with frank jaundice or liver disease being an obvious contraindication. A low incidence of completely reversible jaundice on the basis of intracanicular biliary stasis in association with chlorpropamide therapy has been reported. Accordingly, although transient alterations of alkaline phosphatase are often observed after institution of chlorpropamide therapy, a persistent, serially rising level constitutes an indication for withdrawal of therapy.

Although hypoglycemia of a serious degree has, on occasion, been reported after the administration of tolbutamide, such reactions are more readily produced by overdosage of chlorpropamide. The exaggerated hypoglycemic effect is most likely to occur during the transition period from insulin, but it is a potential danger at any time when there is careless manipulation of dosage. Because of the prolonged action of chlorpropamide, if a hypoglycemic reaction occurs, the patient should be treated with glucose and observed over a period of time to guard against the reappearance of a hypoglycemic episode. To avoid the occurrence of hypoglycemia, the correct dose of chlorpropamide should be given preferably as a single dose with or before breakfast. Chlorpropamide should not be given in the evening without meals. Also, because of its increased potency, chlorpropamide shows a certain similarity of effect to insulin in that the margin of safety between doses producing euglycemia and hypoglycemia is smaller than with tolbutamide. Hence, with chlorpropamide, as with insulin, it is imperative that there be a careful initial adjustment of dosage, as well as adequate orientation of the patients concerning hypoglycemic reactions and their control and the necessity of regular, thorough, follow-up examinations.

It is still too early to make a final assessment of the comparative merits of chlorpropamide and tolbutamide. Presently available evidence, however, would suggest that the advantages of chlorpropamide are threefold: 1. It may be useful in some patients who are originally or who may become unresponsive to tolbutamide. 2. It may make possible a somewhat smoother control of blood sugar. 3. Its prolonged action makes it more convenient to use, i. e., less frequent administration of smaller doses. On the other hand, chlorpropamide has several disadvantages when compared with tolbutamide. These are (1) a slightly higher clinical toxicity and a smaller margin of safety with respect to production of hypoglycemia and (2) the possibility of jaundice.

Dosage

Chlorpropamide is administered orally. The total daily dosage is generally administered as a single dose each morning with breakfast. Occasional cases of gastrointestinal intolerance may be relieved by dividing the daily dose.

The initial daily dosage for middle-aged patients with mild to moderately severe diabetes should be 250 mg. or less. Because the geriatric diabetic patient appears to be more sensitive to the effects of hypoglycemic agents, consideration should be given to starting older patients on smaller amounts of chlorpropamide.

No transition period is necessary when transferring patients from other oral hypoglycemic agents to chlorpropamide therapy. The administration of the other agent may be discontinued at once and therapy with chlorpropamide started. Although insulin therapy should not be stopped abruptly in the severe or brittle diabetic patient or in the patient receiving over 40 units of insulin per day, the majority of middle-aged patients with mild to moderately severe, stable diabetes who receive insulin can be placed directly on chlorpropamide and their insulin therapy discontinued at once. For patients requiring more than 40 units of insulin daily, chlorpropamide therapy may be initiated with a 50% reduction in insulin for the first few days, with subsequent reductions of insulin dependent upon the response to chlorpropamide.

During the period of insulin withdrawal, the patient should be instructed to test his urine for sugar and ketone bodies at least three times daily and report the results daily. In some cases, it may be advisable to consider hospitalization of the patient during the transition period.

Three to five days after initial therapy, the blood level of chlorpropamide reaches a plateau. The dosage may be increased or decreased by 50 to 125 mg. at intervals of three to five days to obtain optimal control.

Most middle-aged patients with moderately severe, stable diabetes are controlled by about 250 mg. of chlorpropamide daily. Patients with mild diabetes may do well on daily doses of 100 mg. or less. Many persons with more severe diabetes may require 500 mg. daily for adequate control. Patients who do not respond completely to 500 mg. will usually not respond to higher doses. Maintenance dosage above 750 mg. daily should be avoided.

Preparations

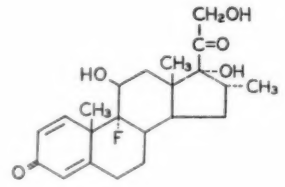
Tablets 100 mg. and 250 mg.
Year of introduction: 1958.

Eli Lilly & Company and Pfizer Laboratories, Division of Chas. Pfizer & Co., Inc., cooperated by furnishing scientific data to aid in the evaluation of chlorpropamide.
***J.Am.Med.Assoc.* 172:57 (Jan. 2) 1960.**

Dexamethasone

Decadron®
Deronil®
Gammacorten®

DEXAMETHASONE (Decadron, Deronil, Gammacorten) is 9α-fluoro-16α-methylprednisolone.—The structural formula of dexamethasone may be represented as follows:



Actions and Uses

Dexamethasone is a synthetic analogue of hydrocortisone, with similar actions and uses. It is the most potent anti-inflammatory glucocorticoid yet available. Laboratory and clinical experience indicate that doses of 0.75 mg. of dexamethasone produce an anti-inflammatory response equivalent to that of about 4 mg. of triamcinolone or methylprednisolone, 5 mg. of prednisone or prednisolone, 20 mg. of hydrocortisone, and 25 mg. of cortisone. However, this greatly increased potency does not necessarily confer upon dexamethasone any special therapeutic advantage over other steroids with essentially the same pharmacological effects. Thus, except for using much smaller doses, therapy with dexamethasone may be expected to give results essentially the same as those anticipated with triamcinolone, methylprednisolone, prednisone, and prednisolone. As with the latter drugs, dexamethasone appears to lack the sodium-retaining and potassium-excreting properties of the earlier gluco-corticoids, cortisone and hydrocortisone. In fact, it may at first have a diuretic effect when substituted for cortisone or hydrocortisone in patients made edematous by these agents. In this respect, dexamethasone is well suited for long-term therapy in which steroid-induced fluid retention and electrolyte imbalance might otherwise become a problem. By the same token, the lack of mineralo-corticoid activity with dexamethasone makes it inferior to cortisone, hydrocortisone or fludrocortisone for replacement therapy in adrenal cortical insufficiency (Addison's disease). Hence, dexamethasone is used principally for its anti-inflammatory and antiallergic effects. It is useful in appropriate cases of rheumatoid arthritis and other collagen diseases, allergic conditions, inflammatory eye diseases, certain leukemias and lymphomas, soft tissue inflammations, hemolytic anemias, and other conditions generally considered responsive to systemic glucocorticoid therapy. Some patients who respond poorly or are intolerant to other steroids may be managed satisfactorily with dexamethasone. As with all drugs of this class, the disadvantages and dangers, particularly since there is a tendency toward repeated use, should be weighed carefully against the benefit to be expected. Prolonged therapy with dexamethasone will suppress the function of the adrenal cortex; although ordinarily a hazard to its use, this property of the drug may be used advantageously in patients with adrenogenital syndrome.

Toxicity and Side-Effects

Although clinical experience is not sufficient to permit quantitative comparisons, it is apparent that side-effects and untoward reactions to dexamethasone are qualitatively similar to those of other glucocorticoids. It would appear from available data that dexamethasone has less tendency to cause salt and water retention and disturbance of glucose metabolism. The drug can cause peptic ulceration, decreased resistance to infection, demineralization of bone with resultant osteoporosis, insomnia, psychic disturbances, rounding of the face, fat deposition, hirsutism, acne, abdominal striae, petechiae, purpura, and amenorrhea. In common with all steroids, except triamcinolone which may cause decreased appetite and weight loss, dexamethasone causes an increase in appetite; weight gain may often be observed during prolonged therapy. The euphoria often seen with other steroids and the aggravation of the diabetic state have not been prominent with this drug. Relative contraindications to therapy with dexamethasone include active, latent, or questionably healed tuberculosis, other acute or chronic infections, peptic ulcer, osteoporosis, fresh intestinal anastomoses, diverticulitis, thrombophlebitis, and psychotic tendencies. Herpes simplex of the eye is an absolute contraindication except when the need for dexamethasone is considered greater than the risk to the function of the eye. The drug should be used cautiously in pregnant women, particularly during the first trimester, to avoid the possibility of postnatal hypoadrenalism in the fetus.

Dosage

Dexamethasone is administered orally. Dosage must be individualized according to the severity of the disease, anticipated duration of steroid therapy, appearance of side-effects, and therapeutic response. In general, the total daily dosage of dexamethasone is about one-fifth that of triamcinolone or methylprednisolone and about one-sixth that of prednisone or prednisolone. In chronic conditions requiring long-term therapy, the lowest dose that will provide adequate, not necessarily complete, relief of symptoms should be used. This is because prolonged administration of high doses may produce unwanted hormonal effects. In life-threatening and other acute conditions, large doses are permissible and may be mandatory for short periods of time. The daily requirement is usually given in three or four divided doses. However, with the exception of acute conditions, administration of the daily requirement in two divided doses provides adequate therapy for some patients both initially and in maintenance.

For rheumatoid arthritis, suppressive doses of 1.5 to 3 mg. per day may be given initially. Dosage is then decreased gradually to the smallest amount that gives the desired degree of symptomatic relief; this may be as low as 0.75 mg. per day Alternatively, therapy may be initiated with small doses (0.75 to 1 mg. per day) and the increased gradually to eventual maintenance levels. For acute, nonfatal conditions such as seasonal asthma and self-limited ocular and dermatological disorders, daily dosages range between 2 and 3 mg. For chronic, potentially fatal diseases such as disseminated lupus erythematosus, pemphigus, and sarcoidosis, the usual initial dose is 2 to 4.5 mg. per day. For acute rheumatic fever, crisis of disseminated lupus erythematosus, and severe allergic reactions, initial doses of 7.5 to 10 mg. or more per day have been used. However, in such acute, life-threatening situations in which rapid onset of action is imperative, consideration should be given to the intravenous use of gluco-corticoids suitable for this route of administration. Massive doses of 10 to 15 mg. per day have been given to patients with acute leukemia, the nephrotic syndrome, and acute pemphigus. For the treatment of adrenogenital syndrome daily doses of 0.5 to 1.5 mg. are used.

Preparations

Tablets 0.5 mg. and 0.75 mg.

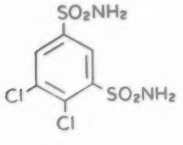
Year of introduction: 1958.

Merck Sharp & Dohme Research Laboratories, Division of Merck & Co., Inc., and Schering Corporation cooperated by furnishing scientific data to aid in the evaluation of dexamethasone.

J.Am.Med.Assoc. 171:2095 (Dec. 12) 1959.

Dichlorphenamide — Daranide®

DICHLORPHENAMIDE (Daranide) is 1,2-dichloro-3,5-disulfamylbenzene.—The structural formula of dichlorphenamide may be represented as follows:



Actions and Uses

Dichlorphenamide is a carbonic anhydrase inhibitor with pharmacological actions similar to, but not identical with, those of acetazolamide and ethoxzolamide. On the basis of its ability to inhibit carbonic anhydrase in vitro and on the basis of dosage requirements for comparable pharmacological effects in human beings, dichlorphenamide appears to be one of the most potent drugs of this class currently available. After oral administration, it causes an increased urinary excretion of electrolytes accompanied by diuresis. Sodium and, to a slightly lesser extent, potassium are the principal cations affected. Of the anions, the excretion of bicarbonate predominates. Thus, dichlorphenamide produces a copious flow of slightly alkaline urine. In contrast to other carbonic anhydrase inhibitors, the drug also causes a definite increase in chloride excretion. As a result, metabolic acidosis is less frequent and less pronounced than with other agents of this type. The diminished likelihood of metabolic acidosis is responsible, in part, for two additional characteristics which distinguish dichlorphenamide from other carbonic anhydrase inhibitors: 1. Patients generally continue to show diuretic effects upon repeated administration of the drug. 2. Its anticonvulsant effects are considerably less than with acetazolamide or ethoxzolamide, thus rendering the drug relatively ineffectual for the treatment of epilepsy.

Dichlorphenamide is well absorbed from the gastrointestinal tract. Its distribution, metabolic fate, and excretion are not known.

Although dichlorphenamide appears to be a moderately effective diuretic agent, its clinical use is presently restricted to the treatment of glaucoma. The drug lowers intraocular pressure in normal and most glaucomatous human eyes by reducing the rate of secretion of aqueous humor. In patients responsive to the drug, intraocular pressure begins to fall within one hour after oral administration, reaches a minimum level within two to four hours, and is maintained at a reduced level for 6 to 12 hours. Dichlorphenamide has been used for short-term administration in the management of acute (narrow angle or angle closure) glaucoma and for the acute phase of secondary glaucoma. It is occasionally successful in patients who are refractory to acetazolamide or ethoxzolamide. In some patients with acute glaucoma, however, neither intraocular pressure nor aqueous flow responds to any form of medical management; in these cases, prompt surgery may be mandatory. In all types of glaucoma, dichlorphenamide may be tried for the short-term preoperative control of intraocular tension.

As with any carbonic anhydrase inhibitor, the long-term use of dichlorphenamide for the treatment of chronic congestive glaucoma or chronic simple (wide-angle) glaucoma should be approached cautiously. At the present time, clinical experience with the drug for this purpose is too limited to permit definite conclusions as to its ultimate usefulness. In long-term use, the possible occurrence of serious electrolyte depletion should be borne in mind.

Irrespective of the type of glaucoma being treated with dichlorphenamide, emphasis should be placed on the concomitant administration of standard miotics, particularly in primary glaucomas. It is conceivable that true hypersecretion glaucoma with no obstruction to outflow could be treated with dichlorphenamide or other carbonic anhydrase inhibitors alone until the cause of the hypersecretion has been removed.

Toxicity and Side-Effects

In the doses required for adequate control of intraocular pressure, the nature and frequency of side-effects due to dichlorphenamide are about the same as those due to acetazolamide or ethoxzolamide. Among these are anorexia, nausea, vomiting, confusion, ataxia, tremor, tinnitus, dizziness, paresthesias, depression, and lassitude. In rare instances, hypersensitivity may be manifested by pruritus, urticaria, and erythematous rash. If therapy is to be prolonged, it is essential to keep a close check on electrolyte balance. Hypokalemia, in particular, must be guarded against, since clinical signs and symptoms of this condition are often insidious in onset. Should this occur, an appropriate potassium salt given orally can usually be administered simultaneously without interfering with the ocular effects; if hypokalemia is severe, further medication should be temporarily discontinued. Dichlorphenamide must be used cautiously in patients with respiratory disorders characterized by a severe reduction in pulmonary ventilation. As with other carbonic anhydrase inhibitors, the drug is contraindicated in patients with hyperchloremic acidosis, adrenocortical insufficiency, and renal failure. Although dichlorphenamide is a sulfonamide derivative, there is no evidence to date of hematopoietic depression or adverse effects on the kidney.

Dosage

Dichlorphenamide is administered orally. The proposed dosage for adults is an initial dose of 100 to 200 mg., to be followed by 100 mg. every 12 hours until the desired response has been obtained. A dosage of 25 to 50 mg. one to three times daily may be employed for maintenance therapy. Adjustment of dosage to the needs of the individual patient is important.

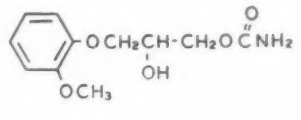
Preparations

Tablets 50 mg.

Year of introduction: 1958.
Merck Sharp & Dohme Research Laboratories, Division of Merck & Co., Inc., cooperated by furnishing scientific data to aid in the evaluation of dichlorphenamide.
J.Am.Med.Assoc. 172:69 (Jan. 2) 1960.

Methocarbamol — Robaxin®

METHOCARBAMOL (Robaxin) is 2-hydroxy-3-*o*-methoxyphenoxypropyl carbamate.—The structural formula of methocarbamol may be represented as follows:



Actions and Uses

Methocarbamol is a centrally acting skeletal muscle relaxant similar in pharmacological properties to mephenesin carbamate. The indications for the use of methocarbamol are the same as for other drugs of this group, but its relative value in comparison with other such agents remains to be established by further clinical trial.

Methocarbamol has been found useful in relieving the acute muscle spasm associated with trauma, herniated intervertebral disks, torticollis, and fibromyositis, and in facilitating reduc-

tion of dislocations of the shoulder. It sometimes reduces the spasticity, but rarely the athetoid movements, of cerebral palsy. Evidence concerning its effect on the tremor and rigidity of paralysis agitans (Parkinson's syndrome) is conflicting. It is relatively ineffective in combating chronic muscle spasm, such as that accompanying chronic arthritis and persistent back pain, or in relieving the spasticity of multiple sclerosis and the contractures of muscular dystrophy.

Plasma concentrations of methocarbamol reach their peak about one hour after oral administration, as compared to 30 minutes for mephenesin. Plasma levels are also more sustained than those of mephenesin when equimolar doses of the two drugs are administered. The greater persistence of methocarbamol in the blood is apparently not caused entirely by slower intestinal absorption, since it can be demonstrated after intravenous injection as well.

The experimental observation that methocarbamol, in small doses, markedly depresses multisynaptic, but not monosynaptic, spinal reflexes suggests that it acts primarily on the internuncial neurons of the spinal cord. However, the fact that it prolongs the sleeping time of animals given hexobarbital indicates an additional effect on the higher centers. Methocarbamol protects animals against the convulsive effects of strychnine, pentylenetetrazol, or electroshock.

Although about 10% of the patients receiving methocarbamol report unpleasant symptoms or reactions, these are usually mild. Drowsiness, vertigo, blurred vision, headache, nausea, fever, and skin eruptions have been observed. Subjective complaints often disappear with continued medication or may be controlled by a reduction in dosage. Intramuscular injection may produce local irritation. Intravenous administration has been followed by flushing, nausea, metallic taste, and, in one patient, by decrease in blood pressure and bradycardia.

In the early trials of methocarbamol, three cases of transient leukopenia, in which the blood cell count returned to normal despite continuation of therapy, were reported. However, in the subsequent extensive use of the drug, no further instances of this complication have been reported. No serious blood dyscrasias have occurred.

Experiments in animals indicate that methocarbamol, upon intravenous administration, may cause intravascular hemolysis. However, it appears to be less active in this respect than mephenesin, and recommended doses, injected slowly, appear to have only minimal, if any, hemolytic action.

Commercial preparations of methocarbamol may utilize polyethylene glycol as a solvent. Since the latter substance has been reported to increase existing acidosis and urea retention in patients with renal impairment, preparations utilizing this vehicle should not be administered to patients with known or suspected renal disease.

There are no known contraindications to the oral use of methocarbamol. However, patients should be advised that drowsiness and vertigo occasionally occur and that, when these symptoms are present, operation of motor vehicles or other activities requiring mental alertness and physical skill may be hazardous.

Dosage

Methocarbamol is administered orally or by intramuscular or intravenous injection. Dosage should be adjusted to meet the requirements of the individual patients. However, for initiating therapy, 1.5 to 2.0 Gm. may be given orally four times daily for 48 to 72 hours. Thereafter, 1.0 Gm. four times daily may be sufficient to maintain any beneficial effects. In children, the oral dosage is proportional to body weight; the total daily dosage should not exceed 30 mg. per pound of body weight.

When given intramuscularly, a single dose, in adults, should not exceed 1 Gm. not more than 500 mg. should be injected in each buttock. The dose may be repeated at intervals of eight hours. Once the desired degree of muscular relaxation has been achieved, substitution of oral therapy is usually desirable.

It is essential that the rate of intravenous injection of 10% solutions of methocarbamol not exceed 3.0 cc. per minute. Care must be taken that extravasation does not occur, since the solutions cause considerable local irritation. No more than 1 Gm. is given in a single injection; the total daily dose should not exceed 3 Gm. Intravenous therapy should not be continued for more than three days in succession.

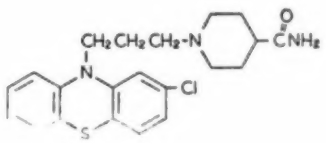
Preparations

Solution (injection) 1 Gm. in 10 cc.; tablets 500 mg.

Year of introduction: 1957.
A. H. Robins Company, Inc., cooperated by furnishing scientific data to aid in the evaluation of methocarbamol.
J.Am.Med.Assoc. 172:60 **(Jan. 2) 1960.**

Pipamazine — Mornidine®

PIPAMAZINE (Mornidine) is 10-[3-(4-carbamoylpiperidino)propyl]-2-chlorphenothiazine.—The structural formula of pipamazine may be represented as follows:



Actions and Uses

Pipamazine is a substituted phenothiazine derivative with actions similar to those of other drugs of this chemical class. Thus, it exhibits both antiemetic and sedative actions. Pharmacological studies in animals indicate that, on a weight basis, pipamazine may be more potent than chlorpromazine in antiemetic activity but less potent in tranquilizing activity. Such studies suggest a relative specificity or increase in antiemetic action in relation to tranquilizing action. Hence, pipamazine is used clinically only for its antiemetic effects. The drug influences nausea and vomiting by an inhibitory action on the medullary chemoreceptor trigger zone; it does not act on the emetic center. After oral administration in human beings, the onset of action of pipamazine is about 30 minutes.

Pipamazine has been employed for the prevention and control of nausea and vomiting due to a variety of causes. These include emesis associated with pregnancy, anesthesia, radiation therapy, nitrogen mustard therapy, and gastroenteritis. In one controlled study, the drug reduced the incidence of vomiting after surgical anesthesia from 10% to 6 %. The remainder of the clinical reports are largely uncontrolled. Nevertheless, it is the clinical impression of most observers that pipamazine is frequently effective for the symptomatic management of nausea and vomiting. Its ultimate usefulness in comparison with other antiemetic agents must await the results of additional controlled studies.

Toxicity and Side-Effects

Doses greater than 10 mg. per day may, in occasional patients, cause mild to moderate sedation. With the exception of drowsiness, however, and, less frequently, postural hypotension, the usual therapeutic doses of pipamazine are well tolerated. Signs of extrapyramidal involvement (muscle spasm and Parkinson-like symptoms) have been encountered at dosage levels far beyond the usual therapeutic range. In occasional instances, abnormal values in certain liver function tests (serum bilirubin, serum transaminase, and sulfobromophthalein retention) have been observed, but overt jaundice or clinical signs or symptoms suggesting hepatic damage have not been attributed to therapy with the drug. Because it is a phenothiazine derivative, however, pipamazine should not be given to patients with known liver disease. For the same reason, it should be withheld in patients with leukopenia

or other evidence of hematopoietic depression, even though there is no evidence that the drug depresses bone marrow function. Since it potentiates the action of other central nervous system depressants, caution is enjoined in the use of pipamazine in patients under the influence of narcotics, barbiturates, alcohol, or general anesthetics. Chronic administration in rats causes arrest of the estrous cycle in the progestational phase and reduction of weight of accessory reproductive organs in both sexes; the clinical significance of these laboratory findings is not known, but it might be important.

Dosage

Pipamazine is administered orally or by intramuscular or intravenous injection. The usual dose for adults by the oral route is 5 mg. every four to six hours; if the drug cannot be retained orally, the same dose may be given intramuscularly. If intravenous administration is necessary, a dose of 5 mg. is injected slowly over a period of five minutes.

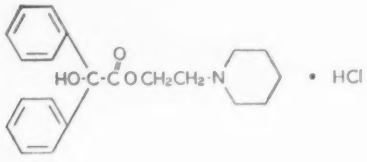
Preparations

Solution (injection) 5 mg. in 1 cc.; tablets 5 mg.

Year of introduction: 1959.
G. D. Searle & Co. cooperated by furnishing scientific data to aid in the evaluation of pipamazine.
J.Am.Med.Assoc. 171:2096 (Dec. 12) 1959.

Pipethanate Hydrochloride — Sycotrol®

PIPETHANATE HYDROCHLORIDE (Sycotrol) is 2-(1-piperidino) ethyl benzilate hydrochloride.—The structural formula of pipethanate hydrochloride may be represented as follows:



Actions and Uses

PIPETHANATE HYDROCHLORIDE (Sqcotrol) is 2-(1-piperstructure to benactyzine hydrochloride, is proposed for use in the management of anxiety and tension accompanied by somatic complaints. It has been reported to be helpful in alleviating cardiac symptoms associated with anxiety, including palpitation, tachycardia, and angina; in the management of peptic ulcer, colitis, spastic colon, hypertension, coronary insufficiency, and menopausal complaints; and in ameliorating the tremors of senility and paralysis agitans. However, clinical experience with the drug is still extremely limited, and careful observations comparing it with other similar agents or with placebos have not been reported. Consequently, although favorable results have been described in the aforementioned conditions, further controlled clinical studies are required for convincing evidence that these results were attributable to the drug or that other drugs might not have given equally good or superior results.

In animals the drug has been shown to exert anticholinergic effects and to modify stress-induced behavior in a manner similar to that of benactyzine hydrochloride. It should be pointed out, however, that if the potency ratios observed in animals prevail in man, usual clinical doses of pipethanate hydrochloride would be expected to provide significantly less anticholinergic activity than customary doses of atropine and to influence behavior to a lesser degree than the usual doses of benactyzine hydrochloride. Pipethanate hydrochloride also possesses potent local anesthetic and quinidine-like atrial antifibrillatory actions, but these properties, demonstrated in the laboratory, have received no clinical application.

Although toxicity studies in animals are inadequate as reported, no undesirable effects, with the exception of drowsiness, have been reported in man. The possibility of serious systemic toxicity, however, has not been thoroughly explored either in animals or in human subjects. Therefore, patients receiving the drug should be carefully observed for untoward effects.

Dosage

Pipethanate hydrochloride is administered orally. The proposed dose is 3 to 6 mg., three times daily.

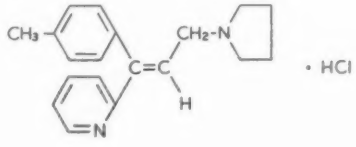
Preparations

Tablets 3 mg.

Year of introduction: 1959.
Reed & Carnick cooperated by furnishing scientific data to aid in the evaluation of pipethanate hydrochloride.
J.Am.Med.Assoc. 171:2097 (Dec. 12) 1959.

Triprolidine Hydrochloride — Actidil®

TRIPROLIDINE HYDROCHLORIDE (Actidil) is *trans*-2-[3-(1-pyrrolidinyl)-1-(p-tolyl)propenyl]pyridine hydrochloride. — The structural formula of triprolidine hydrochloride may be represented as follows:



Actions and Uses

Triprolidine hydrochloride is an antihistaminic agent with actions and uses similar to those of other drugs of this group. (See the general statement on histamine-antagonizing agents in New and Nonofficial Drugs.) After a single oral dose, effects are perceptible within 15 minutes and persist for four to eight hours.

No serious adverse effects have resulted from the clinical use of triprolidine hydrochloride. The incidence of minor side-effects is comparable to that associated with other antihistaminic agents; patients should be advised that drowsiness may occur.

Chronic toxicity studies in animals have disclosed no untoward effects on renal, hepatic, or hematopoietic function. On the basis of a single experiment in which the drug increased the volume and acidity of histamine-induced gastric secretion, it has been suggested that triprolidine hydrochloride be used only with caution in patients with a history of peptic ulcer. However, a similar effect has been observed with other antihistaminic agents, and there is no evidence that triprolidine hydrochloride produces a greater degree of gastric irritation than do other drugs of this group.

Dosage

Triprolidine hydrochloride is administered orally, usually three times a day. The usual single dose for adults is 2.5 mg.; for children over two years of age, 1.25 mg.; and for infants, 0.6 mg.

Preparations

Syrup 0.25 mg. per cc.; tablets 2.5 mg.

Year of introduction: 1958.
Burroughs Wellcome & Co. (U. S. A.) Inc., cooperated by furnishing scientific data to aid in the evaluation of triprolidine hydrochloride.
J.Am.Med. Assoc. 172:59 (Jan. 2) 1960.

POSITIONS

in hospital pharmacy

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The Personnel Placement Service is operated without charge for the benefit of hospitals and pharmacist members of the American Pharmaceutical Association and the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS. The ultimate purpose is the improvement of pharmaceutical services in hospitals, by more adequately fulfilling hospital pharmacy personnel needs and by locating positions which provide challenging opportunities for pharmacists who have indicated an interest in a hospital career.

By participating in the service, the hospital indicates a desire to achieve a pharmaceutical service which meets the Minimum Standard for Pharmacies in Hospitals. A description of the position should be submitted to the Division of Hospital Pharmacy on the forms provided. The hospital will receive applications directly from the applicant. The hospital agrees to reply to each application received and to notify the Division of Hospital Pharmacy when the position is filled.

The pharmacist, by participating, agrees to submit a Personnel Placement Service Information Form to the Division of Hospital Pharmacy. The applicant will then be notified of openings listed with the Service as they become available and can negotiate directly with the hospital if he is interested. It is agreed that the Division of Hospital Pharmacy will be notified as soon as a position is accepted.

A listing of positions open and wanted will be made regularly in the AMERICAN JOURNAL OF HOSPITAL PHARMACY without charge. Neither the name of the hospital offering the position nor the name of the applicant will be listed, except by code. All inquiries should be directed as shown below, including the code number.

Address all inquiries to
Division of Hospital Pharmacy
2215 Constitution Avenue, N. W.
Washington 7, D.C.

positions open

STAFF PHARMACIST—325 bed general hospital located in Pa. Duties include filling requisitions from the various nursing stations for floor drugs and completing specific prescriptions to patients. Forty hour week, vacations, group hospitalization. PO-186

STAFF PHARMACIST—400 bed general hospital located in Mich. Excellent opportunity in an expanding pharmacy program. Liberal benefits. PO-185

ASST. CHIEF PHARMACIST—155 bed general hospital. Duties include filling inpatient prescriptions and assuming full responsibility of pharmacy in the absence of chief pharmacist. Applicant must have B. S. in Pharmacy, be eligible for registration in Ga. and be willing to work on weekends. Forty-four hours per week, 2 weeks' vacation. PO-184

SUPERVISOR OUTPATIENT PHARMACY OR STAFF PHARMACIST—1,000 bed general hospital located in East. Duties include dispensing, supervision of prepackaging, checking stock. B. S. required. PO-183

PHARMACIST—320 bed general hospital located in Pa. To assume direct supervision of the central sterile supply dept., attend meetings concerning central sterile supply, and be responsible for the processing of sterile material and issuing of oxygen. Must have B. S. in Pharmacy and supervisory experience of a central sterile supply. Forty hour week, 2 weeks' vacation. PO-182

CHIEF PHARMACIST—312 bed non-profit community hospital. Male or female with hospital pharmacy experience. Must be qualified and eligible for licensure in Va. Forty to forty-four hour week, 1 month vacation after one year's employment, Blue Cross Insurance, Group Life Insurance Plan. PO-181

CHIEF PHARMACIST—450 bed general medical center. Responsible for complete operation of pharmacy with large outpatient service; supervisory ability needed, experience in developing a hospital formulary required, and must be interested in developing a high level professional service. Will work closely with medical staff and will train personnel. Requirements: male, B. S., minimum 2 years' experience preferably with internship in hospital pharmacy, must be licensed or eligible for licensure in Calif. Forty hour week, 4 weeks' vacation. PO-180

CHIEF AND STAFF PHARMACIST—180 bed general hospital. Duties include compounding prescriptions for hospital patients as well as take-home prescriptions, ordering and pricing drug items. Must be eligible for licensure in Calif. Forty hour week, 2 weeks' vacation after one year, Blue Cross Insurance, sick leave and holidays. PO-179

ASST. CHIEF PHARMACIST—521 bed short-term community hospital. Pharmacy is less than two years old and provides excellent working conditions. Assist chief pharmacist, responsible for manufacturing and dispensing program. Must have B. S. in Pharmacy and be eligible for registration in Pa. Forty-four hour week, 7 days' vacation after 1 year, 14 days' after 2 years and 21 days' after 3 years. Sick leave. PO-178

PHARMACIST—Must be registered for 154 bed Government general hospital primarily for the care of Samoan people. Complete charge of the pharmacy, responsible for dispensing, charges, inventory and ordering through local Medical Supply Dept. Forty hour week with occasional after hour calls. Free medical and hospital care. Transportation furnished. Ten weeks paid leave at the end of two-year contract. Renewable with increase if mutually agreeable. Male or female, single person preferred. Write airmail giving training and experience to: Personnel Officer, Government of American Samoa, Pago Pago, American Samoa.

CHIEF PHARMACIST—264 bed general hospital located in Texas. Plans and directs pharmacy policies, compounds and dispenses medicines, purchases supplies and materials, maintains records and prepares periodical reports. Must be eligible or have M. S. degree. Forty hour week, 2 weeks' vacation. Retirement, sick leave. Hospitalization and life insurance available at no cost to employee. PO-177

CHIEF PHARMACIST—376 (expanding to 600) bed general hospital. Pharmacist will supervise and handle administrative duties in large active pharmacy which has 9 employees. Must have B. S. in Pharmacy, New York State registration or be eligible for licensure. Prefer applicant with at least five years' hospital pharmacy experience with some supervisory ability. Forty hour week, 4 weeks' vacation, insurance, pension plan. PO-176

ASST. CHIEF AND/OR STAFF PHARMACIST—330 bed voluntary general hospital located in Midwest. Duties include compounding and dispensing medications to inpatients, outpatients, and employees. PO-174

STAFF PHARMACIST—Outstanding opportunity in large, well-known hospital in Midwest. Duties include filling prescriptions and floor supply, and some bulk compounding. Eligible for registration in Minnesota; hospital experience preferred. PO-173

PHARMACIST—60 bed hospital located in southwest Colorado needs services of a competent pharmacist. Generous benefits include meals while on duty. Male or female. Excellent quarters available to a single female at very nominal fee in new nurse residency. PO-172

PHARMACIST—800 bed general hospital. Compounds and dispenses medications, sells proprietary medicines, sundries and allied supplies to both in and outpatients. Must be licensed in Indiana or eligible for licensure. Fifty hour week, 2 weeks' vacation after 1 year, 3 weeks' after 3 years and 4 weeks' after 5 years, retirement program entirely free, liberal employee discounts. PO-171

STAFF PHARMACIST—290 bed general medical and surgical city hospital. Duties include compounding, dispensing, manufacturing, and assisting in the purchasing of supplies. Prepares reports and maintains records. Furnishes information concerning medications to physicians and nurses. In absence of associate pharmacist will assist with special duties as assigned by chief pharmacist. Male or female between 23-45 years of age. Ohio registration required. Hospital pharmacy internship preferred. Forty hour week, 2-3 weeks' vacation, 15 days sick leave, retirement plan, credit union, 6 holidays, Blue Cross available. PO-170

STAFF PHARMACIST—200 bed general hospital. Duties include compounding, dispensing and manufacturing. Applicant must have B. S. in Pharmacy and be registered in Conn. Recent graduate acceptable. Forty-four hours per week, two weeks' vacation, pension plan and hospitalization. PO-168

ASST. CHIEF PHARMACIST—102 bed general hospital located in Oregon. Pleasant surroundings in college city of 8,000-20,000 students. Male or female. Must be registered. Forty hour week, 2 weeks' vacation, holidays and sick days. PO-166

ASST. CHIEF PHARMACIST—350 bed general hospital. Assist in training and supervision of employees and in plans and projects of dept. Direct dept. in absence of chief pharmacist. Registration in Ohio and B. S. Degree required. Only male considered, must be over 21 years of age. Forty hour week, 2 weeks' vacation, Social Security, paid holidays, group hospitalization, sick leave. PO-165

STAFF PHARMACIST—100 bed general hospital located in Texas. Assume personal responsibility for accurate filling of prescriptions and supplies, assist in inspecting drugs in nursing stations,

replace stock taken from night emergency container, inspect and refill ophthalmic solution trays from operating room, emergency room and central supply. Female preferred. Must be registered or eligible for registration in Texas. Forty hour week, 2 weeks vacation after one year, paid holidays, 7 days sick leave. PO-164

ASST. CHIEF PHARMACIST—280 bed general hospital. Duties include filling prescriptions and medicine orders from various units, supervise pharmacy clerks, assume administrative responsibility when chief pharmacist is absent. Forty-four hour week, sick leave and six paid holidays. Must be registered in Ill. PO-161

ASST. CHIEF PHARMACIST—293 bed general hospital. Dispensing drugs to nursing stations, filling special orders for patients, ordering stock, keeping records and some manufacturing. Forty hour week, 2 weeks' vacation, 12 days sick leave, 6 holidays, meals while on duty, free hospital care. Must be registered in Md. PO-160

ASST. CHIEF PHARMACIST—235 bed general hospital located 7 miles from Akron, Ohio. Hospital expanding to 310 beds in 1960, pharmacy expanding to serve 500 beds. Filling prescriptions, small volume of manufacturing. Must assume responsibility for pharmacy in the absence of chief pharmacist. Forty hour week, 2 weeks' vacation, hospitalization insurance paid for employee after 6 months probationary period, paid sick leave, 6 paid holidays. PO-159

CHIEF PHARMACIST—103 bed general hospital. Purchasing, receiving and issuing of pharmacy supplies. Taking inventory once a year. Filling out various reports necessary to operation of dept., etc. Must be registered in Wash. State. Forty hours per week, 2 weeks' vacation, 7 paid holidays, 1 sick day per month cumulative to 48, Blue Cross Insurance available. PO-158

STAFF PHARMACIST—269 bed nonprofit general hospital located in Calif. Duties include filling ward orders, individual prescriptions, outpatient prescriptions and narcotic orders. Applicant must have B. S. in Pharmacy, 1 year's experience or preferably hospital pharmacy internship. Willingness to work week ends and nights as required. Male or female. Forty to forty-eigh hour week, two weeks' vacation after one year, 6 paid holidays, 12 days sick leave, hospital insurance plan. PO-157

CHIEF PHARMACIST—190 bed general hospital located in Wis. Pharmacist will have complete control of the pharmacy, responsible for dispensing, charges, inventory and purchasing. Work with medical staff to formulate policies for dept. with administrative approval. Capable of cooperating with the medical staff, helping the medical staff keep abreast of advances in the field, and guiding and directing the nursing staff in their usage of drugs. Thirty-six to forty-four hour week, two weeks' vacation after one year, Municipal Pension Plan, insurance, 10 days sick leave per year accumulative to 30. Must be registered in Wis. PO-156

STAFF PHARMACIST—215 bed general hospital. Compound and dispense drugs, manufacture pharmaceuticals and assist in all other pharmaceutical duties in the pharmacy. B. S. required. Must be eligible for licensure in Pa. Forty hour week, three weeks' vacation, 7 holidays, 10 days paid sick leave, annual physical examinations, merit salary increases. PO-152

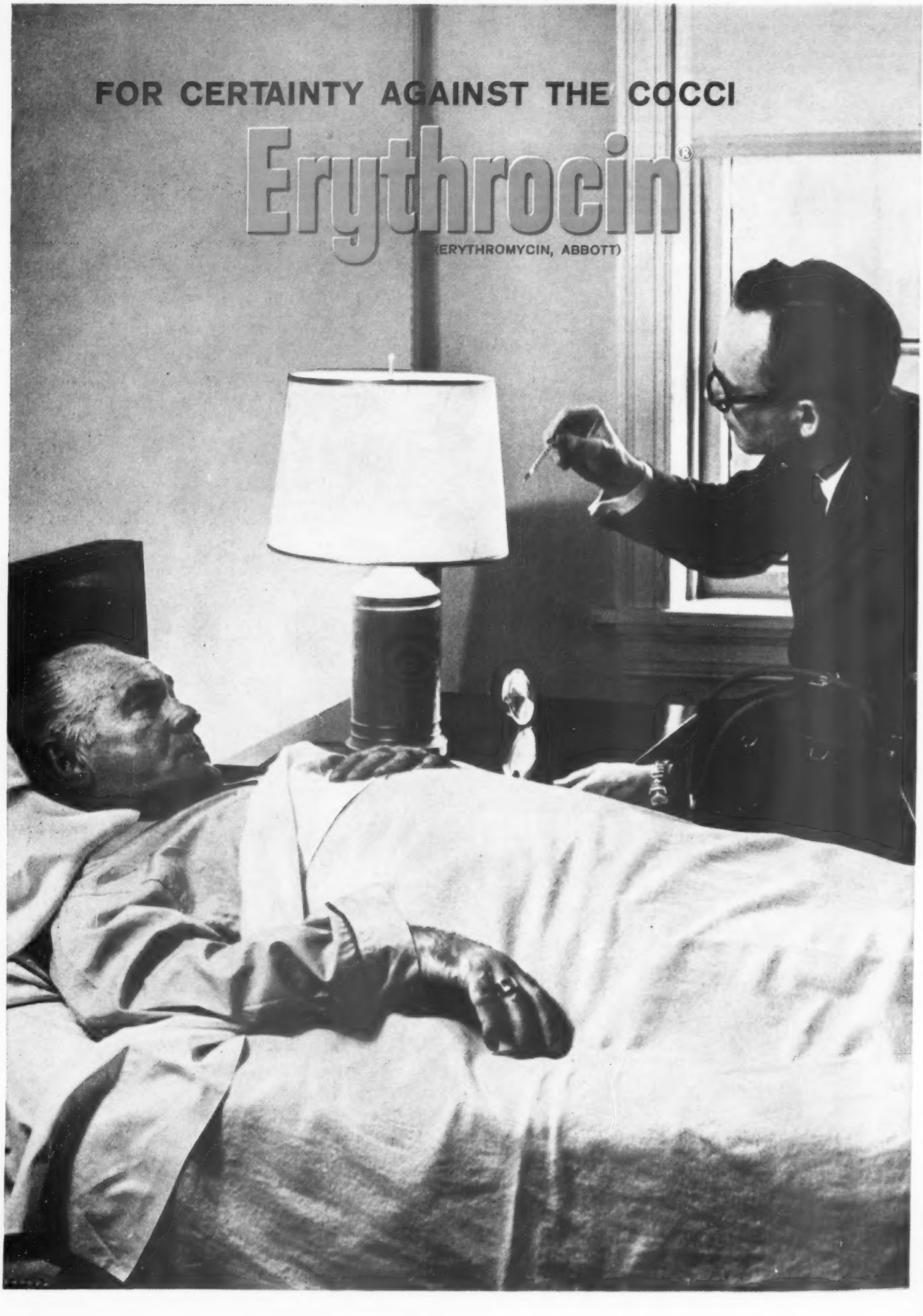
ASST. PHARMACIST—250 bed general hospital. Forty hour week, 2 weeks' vacation, sick leave and 6 paid holidays per year. Must be registered in N. C. PO-150

STAFF PHARMACISTS—Unique, new 400 bed general private hospital where pharmacists join the doctor-nurse team by working in a dispensing unit location on each 100 bed nursing unit or in the central pharmacy. The dispensing unit personnel have responsibility for providing drugs, oxygen, dressing trays, I.V. solutions and similar items. A total of sixteen staff pharmacists is required to staff the hospital. Applicants must be eligible for registration in Calif. Excellent opportunity; generous benefits. PO-148

STAFF PHARMACIST—75 bed general, private hospital located in Ind. State registration required. Male or female. PO-131

CHIEF PHARMACIST—185 bed private nonprofit hospital located in Va. Prefer applicant with hospital pharmacy internship and one year's experience. PO-126

ASST. CHIEF PHARMACIST—425 bed general hospital. Duties include dispensing and supervision of special projects. Prefer male applicant with internship in hospital pharmacy. Unique opportunity to obtain experience. PO-115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STAFF PHARMACIST—500 bed general hospital located in Okla. B. S. required. Forty hour week. PO-95

ASST. CHIEF PHARMACIST—315 bed general hospital. Registration in Iowa required. Experience desirable. Forty hour week, 2 weeks' vacation. PO-92

ASST. CHIEF PHARMACIST—237 bed general hospital in West Virginia. Female desired. Forty-four hour week, 2 weeks' vacation. PO-77

CHIEF PHARMACIST—88 bed hospital located in Pa. Planning expansion to 125 beds for general patients and 40 beds for chronic patients. Possibility for pharmacist to serve as Asst. Adm. in charge of Purchasing, Central Supply, and Store Room. Forty hour week, 2-4 weeks' vacation. Young man preferred. PO-59

ASST. CHIEF PHARMACIST—Large voluntary hospital located in Brooklyn. Must be eligible for registration in N. Y. Supervisory ability needed. Thirty-five hour week, 2 weeks' vacation, 10 days sick leave, 9 holidays. PO-51

positions wanted

CHIEF PHARMACIST—Male, married. Obtained B. S. at Massachusetts College of Pharmacy in 1943. Nine years' hospital pharmacy experience. Prefers to locate in East. Registered in Conn. and Mass. PW-230

STAFF OR CHIEF PHARMACIST—Male, married. B. S. obtained from University of Minnesota in 1953. Served hospital pharmacy internship. Three years' hospital pharmacy experience. Registered in Minnesota. Prefers to locate in the West or Southwest. PW-229

ASST. OR CHIEF PHARMACIST—Male, married. Will obtain B. S. at Philadelphia College of Pharmacy and Science in June, 1960. One year's experience as an apprentice pharmacist at Jefferson Medical College Hospital. Will locate anywhere. Expects to become registered in Pa. first, but willing to take state board examination in any state. PW-228

PHARMACIST—Male, married. B. S. received at Howard College of Pharmacy in 1956. Served hospital pharmacy internship. Two years' hospital pharmacy experience. Prefers to locate in Florida. Registered in Florida and Alabama. PW-227

STAFF PHARMACIST—Male, B. S. received at Massachusetts College of Pharmacy in 1950. Has completed academic work at Medical College of Virginia for M. S. Degree. Served hospital pharmacy internship. Three years' hospital pharmacy experience. Registered in Massachusetts and Washington, D. C. PW-226

PHARMACIST—Female, single. M. S. received at University of Maryland in 1951. Served hospital pharmacy internship. Five years' hospital pharmacy experience. Prefers to locate in New Jersey, registered in Pa. and Mo. PW-225

ASST. CHIEF OR CHIEF PHARMACIST—Male, married. B. S. received at Detroit Institute of Technology in 1950. Four years' hospital pharmacy experience. Prefers to locate in Michigan; registered in Michigan. PW-224

STAFF PHARMACIST—Female, single. Received B. S. at Auburn University in 1952. Three years' hospital pharmacy experience. Prefers Florida, registered in Alabama. PW-223

CHIEF PHARMACIST—Male, married. B. S. received at University of Wisconsin in 1957. Four years' hospital pharmacy experience. Prefers to locate in Wisconsin; registered in Wisconsin. PW-222

ASST. CHIEF OR CHIEF PHARMACIST—Male, married. Received B. S. at Medical College of South Carolina in 1950. Four years' hospital pharmacy experience. Prefers Southeast section of country. Registered in N. C. and S. C. PW-221

CHIEF PHARMACIST—Male, single. Received M. S. at University of Michigan in 1957. Six years' hospital pharmacy experience. Served hospital pharmacy internship. Will locate anywhere. Registered in Mich. and Ohio. PW-220

STAFF PHARMACIST—Female, single. B. S. received at Purdue University in 1958. One and one-half years' hospital pharmacy experience. Registered in Indiana. Prefers to locate in East or Midwest. PW-219

CHIEF PHARMACIST—Male, single. B. S. received in 1952 at Mass. College of Pharmacy. Seven years' hospital pharmacy experience. Registered in Mass. Will locate anywhere. PW-218

STAFF OR CHIEF PHARMACIST—Male, single. B. S. received in 1952 at St. Louis College of Pharmacy. Two years' hospital pharmacy experience. Registered in Mo. Prefers West Coast, particularly Calif. PW-217

ASST. CHIEF OR STAFF PHARMACIST—Female, single. B. S. received at University of Saskatchewan in 1954. Three years' hospital pharmacy experience. Registered in Canada. Would prefer to locate in Southeastern or Western part of U. S. PW-216

CHIEF PHARMACIST—Male, married. Will receive M. S. in June, 1960 at the State University of Iowa. Served hospital pharmacy internship. Registered in Iowa, prefers to locate in the northern Midwest. PW-215

ASST. CHIEF OR CHIEF PHARMACIST—Male, married. B. S. received in 1954 at the Southwestern State College in Okla. Served hospital pharmacy internship at Springfield City Hospital, Springfield, Ohio. Three years' hospital pharmacy experience. Registered in Okla., prefers to locate in Southwest. PW-214

CHIEF PHARMACIST—Male, married. M. S. received from Philadelphia College of Pharmacy and Science in 1958. Served hospital pharmacy internship. Four year's hospital pharmacy experience. Presently completing military obligations. Will locate anywhere and will be available after July, 1960. Registered in Ohio. PW-210

ASST. CHIEF OR STAFF PHARMACIST—Female, single. B. S. Extensive hospital pharmacy experience. Registered in Idaho, Alaska, Ohio and Oregon. Prefers Seattle, Wash. or Northwest section of country. PW-209

CHIEF PHARMACIST—Male, married. Received B. S. in 1957 at Brooklyn College of Pharmacy. Over one year hospital pharmacy experience. Registered in N. Y. and Ill. Prefers East. PW-207

ASST. CHIEF PHARMACIST—Male, single. B. S. received in 1956 at Columbia University College of Pharmacy. Served hospital pharmacy internship. Two years' hospital pharmacy experience. Registered in N. Y. Prefers New York City. PW-206

DIRECTOR OF PHARMACY SERVICE AND/OR CHIEF PHARMACIST—Male, married. Served hospital pharmacy internship and received M. S. in Hospital Pharmacy from the University of Mich. in June, 1959. Seven years' hospital pharmacy experience. Registered in Ill. and Mich. Will locate anywhere. PW-205

CHIEF PHARMACIST—Male, married. M. S. received from Philadelphia College of Pharmacy and Science in 1957. Served hospital pharmacy internship. Over four years' hospital pharmacy experience. Registered in Nebr., Ky., Iowa, and Pa. Prefers Midwest. PW-204

STAFF PHARMACIST—Female, single. B. S. Seven years' hospital pharmacy experience. Southwest section of country preferred. Registered in Ala. and Ga. PW-199

ASST. CHIEF OR CHIEF PHARMACIST—Male, married. B. S. received at Philadelphia College of Pharmacy and Science, 1956. Two and one-half years' hospital pharmacy experience and six years' experience in manufacturing, mainly parenterals. Presently working in Nicaragua. Will locate anywhere in U. S. PW-197

CHIEF PHARMACIST—Male, married. B. S. received in 1953. Four years' hospital pharmacy experience. Prefers Eastern part of country. Registered in Pa. and N. Y. PW-195

CHIEF PHARMACIST—Male, married. M. S. Hospital experience. Prefers to locate in East. Registered in N. Y., Mich., N. J., and Fla. PW-184

ASST. CHIEF OR CHIEF PHARMACIST—Male. B. S. received in 1954. Desires to locate in Mich., Ohio or Ill. Registered in Mich. PW-177

PHARMACIST—Female. Graduate of the University of Idaho, 1954. Registered in Ill. Hospital experience. Prefers Chicago area. PW-166

CHIEF OR ASST. CHIEF PHARMACIST—Female. B. S. and M. S. Purdue University. Ten years' hospital pharmacy experience. Registered in Ind. and Ky. PW-164

PHARMACIST—Male. Registered in La. and Mo. Experienced. Prefers Midwest. PW-161

ASST. CHIEF PHARMACIST—Male, single. Registered in N. Y. and Vt. Served hospital pharmacy internship, now employed part-time staff pharmacist. Prefers Eastern part of country. Has M. S., four years' hospital pharmacy experience. PW-154

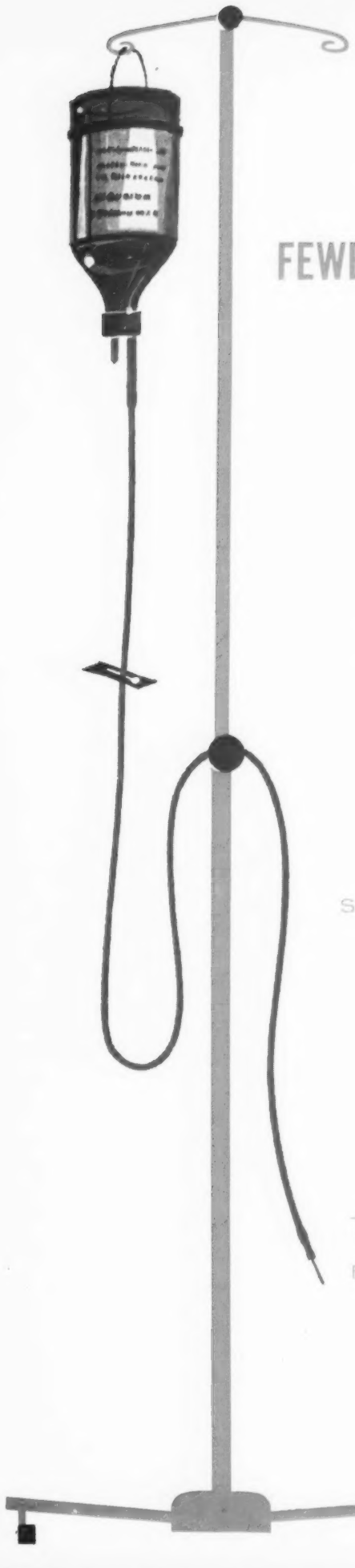
CHIEF PHARMACIST—Male, married. B. S. ten years' hospital pharmacy experience. Registered in Mass., Ill., Mo., Ky., Tenn., and Va. PW-150

PHARMACIST—Male, single. B. S. pharmacy, June 1959. Prefers to locate in East. PW-149

ASST. CHIEF OR CHIEF PHARMACIST—Single, male. Registered in D. C., Ill., Md., and Pa. Graduate University of Pittsburgh in 1953, experience in research. Prefers North and East. PW-148

ASST. DIRECTOR OR DIRECTOR OF PHARMACY SERVICES—Male, single. B. S. Retail and five years' hospital experience. Registered in Ill. PW-119

CHIEF PHARMACIST—Female, single. Registered in Pa. and Ohio. Twelve years' experience as chief pharmacist. Desires to locate in Pa. or Ohio. PW-111



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1. 1958 Report of American Red Cross Joint Blood Council
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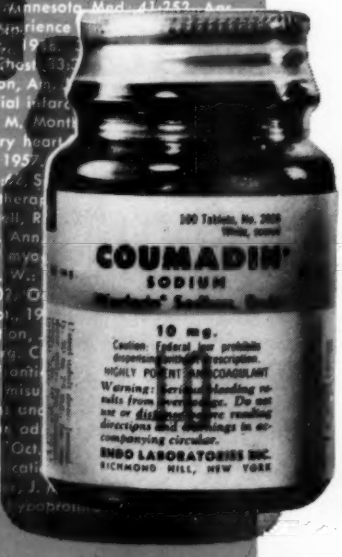

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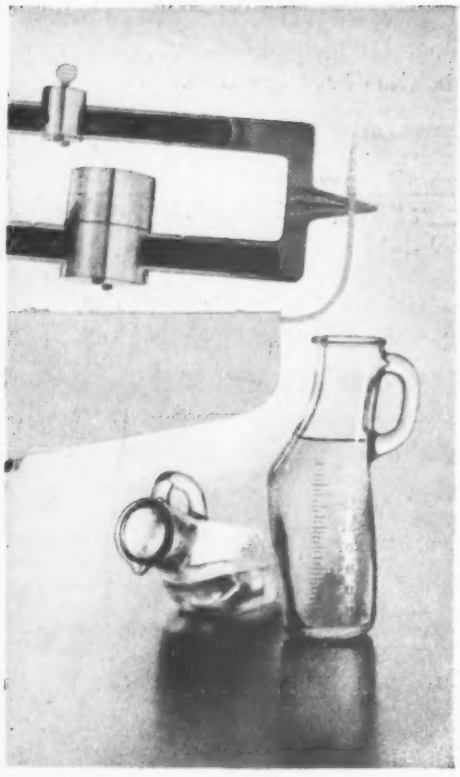

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5. Patients transferring from chlorothiazide to Esidrix frequently experience additional loss of retained body fluid and/or lower blood pressure levels.

6. In most cases, Esidrix permits moderation in severe sodium restriction, makes meals more palatable.

Complete information available on request.

Esidrix®

(hydrochlorothiazide CIBA)

improved analog of chlorothiazide,

a product of CIBA research

CIBA

SUMMIT, N. J.

SUPPLIED: *Tablets*, 25 mg. (pink, scored) and 50 mg. (yellow, scored).

SINGOSERP® (syrosingopine CIBA)
SERPASIL® (reserpine CIBA)
APRESOLINE® hydrochloride (hydralazine hydrochloride CIBA)

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